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## THE SEPARATION OF SOME TERPENOID COMPOUNDS BY GAS-LIQUID CHROMATOGRAPHY<sup>1</sup>

E. VON RUDLOFF

### ABSTRACT

A study has been made of the degree of separation of mixtures of some terpene hydrocarbons, some of their oxygenated derivatives, two sesquiterpene alcohols, and three monophenols on a variety of columns. Temperature and sample size affected the degree of separation and the solid support Chromosorb W, a calcined diatomaceous earth, was found to combine the advantages of Celite and C-22 firebrick without causing decomposition of the sample at higher temperatures. When Craig polyesters were used as liquid phases, separations equal to those obtained on polyethylene glycol were realized with the added advantage that these produced columns which are stable at 190 to 220° C. Consequently, sesquiterpene alcohols and monophenols were also separated successfully. Another useful liquid phase for both low and high temperatures was found in a meta-linked polyphenyl ether. Squalene was found to be an efficient liquid phase for the separation of terpene hydrocarbons at 130° C and lower. The possible application of the present findings for preparative work is discussed.

### INTRODUCTION

A general method for the separation of small amounts of closely related terpene hydrocarbons, some of their oxygenated derivatives as well as some higher boiling sesquiterpene alcohols and monophenols, was required in this laboratory. Such mixtures often have a narrow range of boiling points and separation by fractional distillation not only requires large amounts, but frequently fails to produce pure components. Gas-liquid chromatography (GLC) offers considerable advantages over fractional distillation when quantities of 0.01 to 0.1 g are required, and has in several instances been extended to the gram scale. This technique was, therefore, studied in some detail to find suitable conditions for complete separation of such terpenoid mixtures on a 0.1- to 1-g scale. The experiments were carried out with a Beckman GC-2 chromatograph, using helium as carrier gas, a thermal conductivity cell as detector, and 6-foot columns of 6-mm inner diameter.

Successful separations of terpenoid compounds by GLC have been described in the literature. Bernhard (1) separated five monoterpene hydrocarbons on 20-foot polyethylene glycol and *n*-octyl phthalate columns, but obtained poor results when silicone fluid, Apiezon L, or high vacuum grease was used as liquid phase. Bayer *et al.* (2) used hydrogen as carrier gas and obtained a fair degree of separation for a large variety of terpenoid compounds on columns containing silicone vacuum grease to which alkali capronates had been added. Cvrkal and Janák (3), also using hydrogen, obtained good results for

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terpene hydrocarbons on dimethylsiloxane and proposed glycerol for oxygenated compounds. The use of hydrogen as carrier gas for mixtures containing unsaturated compounds may create difficulties, since activated centers of the solid support could catalyze phases for the separation of many terpene hydrocarbons, but their retention times of 80 minutes and more are rather high. These authors discuss some of the difficulties encountered in the analysis of essential oils and point out the need for polar liquid phases which can be used at 150° C or higher to fractionate oxygenated derivatives. This has been found in the present study in adipate polyethylene glycol, succinate ethylene glycol, and phthalate ethylene glycol polyesters (Craig polyesters) and in a *m*-linked polyphenyl hydrogenation. Liberti and Cartoni (4) used silicone and tricresyl phosphate as liquid ether. Columns with polyethylene glycol were also used by Stanley (5) and Eglington *et al.* (6) and recently Westaway and Williams (7) have separated almost completely  $\alpha$ - and  $\beta$ -pinene,  $\alpha$ - and  $\gamma$ -terpinene, and limonene on a 6-foot Apiezon M column with nitrogen as carrier gas.

From the data contained in the above communications and in the monograph by Keulemans (8) it was concluded that silicone-type columns could be used for a wide range of compounds at lower and higher temperatures with a fair degree of separation. Far better separation could be expected with polyethylene glycols but the temperature limit of 100 to 130° C (8) would limit its application. These two types of liquid phases were, therefore, used to study the effect of the various physical factors involved and to compare the degree of separation obtained with polyethylene, squalene, Apiezon M, polystyrene, a polyphenyl ether, polyesters of adipic, succinic, and phthalic acids (Craig polyesters), a polyamide, and diglycerol as liquid phases. *d*-Limonene, the mixture of *p*-menthadienes produced by dehydration of  $\alpha$ -terpineol with oxalic acid as catalyst (9), and a synthetic mixture containing *d*-limonene, 1,8-cineole, fenchone, citronellal, camphor,  $\alpha$ -terpineol, citronellol, and bornyl acetate were used as test compounds. The sesquiterpene alcohols, occidantalol and eudesmol, and the monophenols, anethole, eugenol, and isoeugenol, were used for the chromatographic studies at higher temperatures.

Initial experiments in the present study showed that a number of factors influencing the separation of terpenoid compounds have not been described fully in the literature. Also, most of the liquid phases used to date for this purpose, except the rather inefficient silicone type, cannot be used above 100 to 130° C for any length of time. Furthermore, the above communications are mainly concerned with qualitative determinations and do not give the most favorable conditions for preparative separations. The present investigation was therefore extended to cover the effect of sample size, temperature, flow rate, nature of solid support, and the ratio of solid support to liquid phase, as well as a search for liquid phases which could be used successfully for the wide range required. The results obtained in this study show that sample size, temperature, and, to a lesser degree, the solid support can affect the degree of separation. Some of the liquid phases tested gave poor results when samples of 5  $\mu$ l or more were used, yet gave excellent separation with 2  $\mu$ l or less, making these columns useful for analytical work. Two types of liquid phases, Craig polyesters and a polyphenyl ether, could be used equally well at 190–220° C or at lower temperatures. An adipic acid – polyethylene glycol polyester was found to give separations equal to, or better than, those obtained on a polyethylene glycol (Carbowax 400), besides being suitable for high temperature separations, and proved to be the best general purpose column for up to 50  $\mu$ l of terpenoid compounds investigated thus far.



## EXPERIMENTAL

*Apparatus*

A Beckman GC-2 chromatograph equipped with a fraction collector (No. 92730) and a heated inlet (suitable for injection of up to 2 ml) was used in conjunction with a Bristol Dynamaster strip-chart recorder (0.05- to 1.05-mv scale). The chart speed was 0.5 inch per minute and the flow rate of helium carrier gas was measured at the exit by the soap bubble method. Samples were introduced with a Beckman liquid sampler (No. 224000) which allowed the accurate injection of 1.5 to 80  $\mu$ l quantities. The column exhaust was at atmospheric pressure (710–715 mm Hg) whereas the pressure at the column inlet was varied to give the desired flow rates.

*Solid Support and Chemicals*

Celite 545 was water-washed to remove the fines, then acid-washed, neutralized with bicarbonate solution, washed with water, and dried. C-22 Firebrick (60–80 mesh) was prepared by wet milling, drying, and sifting of commercial firebrick. Chromosorb W, a flux-calcined diatomaceous earth, produced by Johns-Manville, was obtained commercially. Silicone high vacuum grease (Dow Corning), squalene (90%, Eastman Chemicals), Carbowax 400 (Carbide and Carbon Chem. Co.), the polyphenyl ether *m*-bis(*m*-phenoxyphenoxy)-benzene (Monsanto Corp.), Apiezon M (Metropolitan-Vickers Electrical Co.), and diglycerol (Colgate-Palmolive Co.) were also obtained from commercial sources. The Craig polyesters were kindly supplied by Dr. B. M. Craig and were prepared by reaction of adipic acid with polyethylene glycol (Carbowax 400) and 1% diglycerol as plasticizer and succinic or phthalic acid with ethylene glycol (10). The succinate polyester (SEG) was a solid having m.p. 96–100° C, whereas the adipic (APEG) and phthalate (PEG) polyester were viscous liquids.

Commercial samples of liquid terpenes and oxygenated derivatives were purified by fractional distillation and for critical work by GLC, using the Carbowax 400 or APEG polyester columns. Collection of the samples was carried out with the detector current reduced from 250 ma to 100 ma or completely turned off. The refractive indices of the samples thus obtained are shown in Table I.

TABLE I  
Refractive indices of terpenoid compounds

	Boiling point (°C)	$n_D^{20}$	
		Purified by distillation	Purified by GLC
$\alpha$ -Pinene	155–156	} 1.4684	1.4671
$\beta$ -Pinene	—		1.4793
$\alpha$ -Phellandrene	175–176	1.4764	1.4730
$\alpha$ -Terpinene	173.5–174.5	—	1.4780
<i>d</i> -Limonene	176–177	1.4731	1.4722
1,8-Cineole	174.5	1.4583	1.4578
Fenchone	192–193	1.4646	—
Citronellal	205–206	1.4527	—
$\alpha$ -Terpineol	219.8	1.4829	1.4830
Citronellol	222	1.4568	1.4560
Bornyl acetate	223–224	1.4643	—

Eudesmol, m.p. 82–84° C,  $[\alpha]_D +32^\circ$ , was obtained by crystallization and sublimation of a commercial sample (Plaimar Ltd., Perth, Australia) which was obtained from

*Callitropsis araucarioides* Compt. Occidentalol, m.p. 95–96° C,  $[\alpha]_D +363^\circ$ , was obtained from the neutral extractives of the heartwood of *Thuja occidentalis* L. as described by Nakatsuka and Hirose (11).

The mixture of *p*-menthadienes obtained by dehydration of  $\alpha$ -terpineol (9) was prepared by refluxing oxalic acid (120 g) in water (240 ml) with  $\alpha$ -terpineol (40 g) for 6 hours. The mixture was steam-distilled, the distillate extracted with ether, and the ethereal solution was dried over calcium chloride. The mixture of terpene hydrocarbons was used as such after the solvent had been evaporated.

#### *Packing of Columns*

The liquid phase (2.5 g) was dissolved in a volume of low-boiling solvent (50 ml chloroform) which is equal to that of the solid support. This solution was placed into a high, narrow beaker or cylinder and the solid support (12.5 g) was added with stirring. Stirring was continued for 3 to 5 minutes after addition and the mixture was spread on a shallow stainless steel tray. After the solvent had evaporated, the residual material was dried *in vacuo* at 60–70° C for about 1 hour. The dried material was poured in small aliquots with tapping into 6-mm inner diameter copper tubing of 6-foot length, taking note of the weight of mixture added. The column was closed on each end with a small glass wool plug and coiled into a 5- to 7-in. diameter coil. It was allowed to equilibrate at the desired temperature and flow rate of helium gas (0.5 to 1.5 hours). Injection of samples was begun when the recorder maintained a steady base line.

When polyethylene (obtained by cutting polyethylene reagent bottles into small pieces) was used as liquid phase, it was dissolved by refluxing in a minimum volume of petrol (b.p. 154–202° C). The solid support was added to the hot solution as above and the drying time was extended to 5 hours.

### RESULTS AND DISCUSSION

#### *Initial Experiments*

Optimum conditions for each type of column were obtained by trial and error. Columns having Celite 545 as solid support were found to require higher temperatures and inlet pressures than those with C-22 firebrick, but the latter caused decomposition of some compounds at higher temperatures, especially aldehydes and tertiary alcohols. Liberti and Cartoni (4) report that Stermachol, a material similar to C-22 firebrick, is not suitable for terpene alcohols, and used inactivated Celite instead. A more suitable solid support was found in Chromosorb W, which combined the advantages of firebrick without causing decomposition. This support was, therefore, used in all subsequent experiments.

For preparative work a high ratio of liquid phase to solid support is desirable (8, 12), but in the present study the degree of separation deteriorated when 20% or more liquid phase was used. A ratio of 1:6 was found to give consistently good results.

Polyethylene, Apiezon M, polystyrene, and a polyamide (Zytel) gave inferior results and these were not further studied. Solid compounds, such as the SEG polyester (m.p. 96–100° C), gave poor separations below their melting or softening point.

#### *Effect of Physical Factors*

The effect of temperature on the degree of separation of the mixture of *p*-menthadienes on the Carbowax column is shown in Fig. 1. Contrary to the report of Bernhard (1), the effect was found to be considerable. Keulemans (8), from theoretical considerations, also considers the effect to be important. The separation at 80° C, the lowest feasible tem-

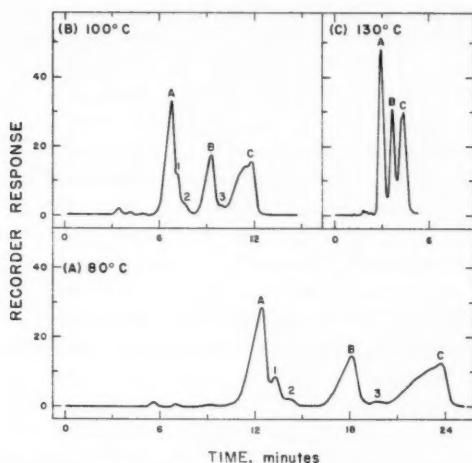


FIG. 1. Separation of the mixture of *p*-menthadienes on the Carbowax column at (A) 80° C and 43.5 ml helium per minute, (B) 100° C and 42.8 ml helium per minute, (C) 130° C and 41.9 ml helium per minute.

perature, was by far the best (Fig. 1(A)), even though the curves are skewed. From a preparative point of view skewing of curves is not detrimental, but is less satisfactory for quantitative calculation. The collection of fractions at the lowest possible temperature has the additional advantage of minimizing the danger of thermal decomposition or rearrangements.

Changes in the flow rate of the carrier gas over the practical range of about 10 to 400 ml (8) did not effect the degree of separation noticeably, which is in agreement with the considerations of Keulemans (8) and the findings of Bernhard (1). Thus, the flow rate was adjusted to give optimum separations at as low a temperature as possible.

The effect of sample size on the retention time of each component was found to be considerable. Table II shows the retention times obtained for *d*-limonene on various columns when samples of 1.5 to 50  $\mu$ l were injected at optimum temperatures and flow rates. From these results it is evident that an increase in sample size above 1 to 3  $\mu$ l

TABLE II  
Effect of sample size on the retention time (in minutes) of *d*-limonene

Column (liquid phase)	Temp. (°C)	Flow rate (ml He/min)	Sample size ( $\mu$ l)							Initial emergence of peak (1.5–50 $\mu$ l)
			1.5	3	5	10	20	40	50	
Silicone (washed)	130	50.5	5.4	5.5	5.6	6.05	6.7*	7.4*	7.8†	4.6–5.0
Silicone (washed)	Duplicate run		5.5	5.6	5.7	6.1	6.8*	7.5*	7.8†	4.7–5.1
Squalene	130	74.2	15.5	15.5	15.6	16.3	17.2*	18.2†	19.0†	14.0–14.3
Carbowax 400	130	46.8	2.85	2.9	2.9	3.0*	3.4*	3.9†	—	2.4–2.5
Polyphenyl ether	130	53.6	6.4	6.55	6.7	6.9*	7.55†	8.1†	—	5.2–5.6
SEG polyester	100	25.0	4.75	4.95	5.35	6.3*	8.2†	—	—	3.6–4.0
PEG polyester	130	41.6	3.95	4.0	4.1	4.3	4.65*	5.25*	5.4†	3.35–3.45
PEG polyester	100	43.5	5.1	5.2	5.5	6.0	6.9*	8.2†	9.0†	3.85–4.25
Diglycerol	80	20.0	2.6	2.75*	3.8†	—	—	—	—	1.2–1.8

\*Skewing clearly visible. †Excessive skewing of peak.

produces considerable delays in the emergence of a peak maximum, and this is accompanied by broadening of the peaks. This is in agreement with the findings of Bens and McBride (13), those obtained by Porter *et al.* (14) with gaseous samples, and those obtained by Bethea and Smutz (15) with aliphatic alcohols on a butyl phthalate column. The latter authors report the optimum sample size for 6-mm diameter columns to be from 4 to 12  $\mu$ l and detected overloading above 20  $\mu$ l. Thomas (16) found the optimum for liquid samples to be 30–70  $\mu$ l. Table II shows that different types of columns have different capacities, silicone and APEG polyester allowing samples of up to 40  $\mu$ l size, although skewing became noticeable with 10–20  $\mu$ l samples. Diglycerol has too low a capacity to be attractive for preparative work, but the other liquid phases may be useful since they have a fair capacity and different separation properties.

The fact that larger samples cause a considerable delay of peak maxima has important consequences for both analytical and preparative work. In the former, an unknown peak is often identified by comparing its retention time with those of known compounds run under identical conditions (8). This is only permissible if the sample size of the unknown and known compounds are nearly the same. The technique of adding the known compound to the unknown (8) may be preferred, but actual isolation and comparison of physical constants (e.g., the infrared spectrum) would seem to be a more reliable means of identification. Another alternative is to make use of the fact that the initial emergence time of a peak remains practically constant with different sample sizes up to where the column becomes badly overloaded (14, Table II). However, this can be used only when all peaks are completely separated from one another.

From a preparative point of view the delay of the peak maximum and broadening of the peak caused by a larger sample is not detrimental, provided skewing or broadening does not cause an overlap with neighboring peaks. Even then, an overloaded column may still produce pure fractions if center cuts are collected. The use of columns having larger diameter (12, 17, 18, 19) did not give the same degree of separation as was obtained on the corresponding 6-mm columns when larger samples (50  $\mu$ l or more) were used. Also, because of the higher flow rates required in larger diameter columns the consumption of helium gas was found to be considerable and it was found more advantageous to carry out repeated runs of 25 to 50  $\mu$ l on the 6-mm diameter columns. Since most columns required only 15–30 minutes for each run, the collection of 0.1 to 0.5 g of a desired fraction was possible within half a day. When such fractions were collected with a normal detector current of 200 to 250 ma, these were yellowish and on rechromatographing the material, typical decomposition peaks were recorded besides the normal symmetrical peaks for the pure compounds. This difficulty was overcome in most instances by using a detector current of 100 ma, which was sufficient for samples of 20  $\mu$ l or more. Only in exceptional cases, e.g.  $\alpha$ -pinene or tertiary alcohols, was it necessary to carry out preparative runs without the detector, i.e. fractions were collected at times determined previously in a run of the same sample size with the detector current on. A possible means of overcoming the necessity of "blind" runs may be to construct a bypass system, similar to those used with detectors other than the thermal conductivity type.

#### *Separation Obtained with Various Liquid Phases*

Terpene hydrocarbons were separated most successfully on columns containing squalene, APEG polyester, and polyphenyl ether, separations being in the same order as those obtained on Carbowax 400 and superior to those obtained on silicone (see Table III). Each column appears to offer slight advantages for one or another compound, a finding which was especially apparent in runs with the complex *p*-menthadiene mixture

TABLE III  
Relative retention times (*d*-limonene = 1) of terpene hydrocarbons

Column (liquid phase)	Silicone	Squalene	Carbowax	Polyphenyl ether	APEG polyester
Temperature (°C)	100	100	100	100	100
Flow rate (ml He/min)	50.5	74.2	42.8	92.4	26.3
<i>d</i> -Limonene (retention time in minutes)	16.75	15.4	8.0	13.2	15.6
$\alpha$ -Pinene	0.57	0.52	0.40	0.39	0.39
$\beta$ -Pinene	0.72	0.69	0.59	0.59	0.61
$\alpha$ -Phellandrene	0.84	0.83	0.79	0.81	0.82
$\alpha$ -Terpinene	0.92	0.88	0.825	0.88	0.88

(Figs. 1 and 2). The squalene column is unstable at 130° C for prolonged periods of time, and an efficient aliphatic polyunsaturated liquid phase which is stable at 130° C or higher is still lacking.

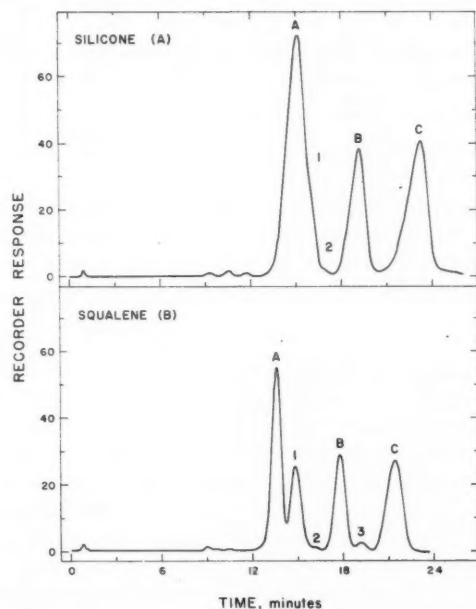


FIG. 2. Separation of the mixture of *p*-menthadienes on (A) silicone (at 100° C and 50.5 ml helium per minute), (B) squalene (at 100° C and 74.2 ml helium per minute).

Resolution of the mixture of *p*-menthadienes on the silicone column (cf. Fig. 2(A)) shows three major peaks A, B, and C, with an indication of further constituents at 1 and 2. The squalene (cf. Fig. 2(B)) and the Carbowax columns (cf. Fig. 1) clearly showed three additional components, 1, 2, and 3, and on the latter column peak C appears to be composed of two compounds in about equal amounts. A very similar separation was obtained with the APEG and SEG polyester columns, whereas the polyphenyl ether column gave the same resolution except that C appeared as a single peak. The best resolution of A, which corresponds to  $\alpha$ -terpinene, was obtained on the squalene column, separation from impurity 1 being complete. From these results it follows that the com-



plex mixture of *p*-menthadienes obtained by dehydration of  $\alpha$ -terpineol cannot be resolved by one column alone, but requires successive fractionation on the squalene and polyester columns. For analytical purposes longer columns or the very efficient Golay columns (20, 21) may have to be used. Peak C presents a problem and its composition, as well as the chemical identification of the other components will be the subject of another communication.

TABLE IV  
Relative retention times (*d*-limonene = 1) of various monoterpenoid compounds

Column (liquid phase)	Silicone	Squalene	Carbowax	Polyphenyl ether	Polyesters		Diglycerol
					APEG	SEG	
Temperature ( $^{\circ}$ C)	130	130	130	130	130	100	100
Flow rate (ml He/min)	30.0	74.2	42.0	53.6	41.6	26.3	20.0
Inlet pressure (mm Hg)	1531	2029	1531	1531	1531	1531	1014
Retention time of <i>d</i> -limonene	8.3	15.5	3.15	6.0	3.8	2.0	1.5
Specific retention volume $V_g$	19.1	27.2	19.1	23.0	15.9	9.0	8.9
1,8-Cineole (b.p. 174 $^{\circ}$ )	1.1	0.95	1.25	1.2	1.25	1.05	1.5
Fenchone (b.p. 192 $^{\circ}$ )	1.4	—	3.0	2.2	2.9	3.0	3.2
Citronellal (b.p. 205 $^{\circ}$ )	2.0	—	3.8	3.0	3.65	4.2	3.25
Camphor (sublimes)	1.95	—	5.15	3.7	5.1	5.6	6.4
$\alpha$ -Terpineol (b.p. 220 $^{\circ}$ )	2.45	—	11.6	4.7	10.95	11.5	6.6
Citronellol (b.p. 222 $^{\circ}$ )	3.1	—	20.2	4.45	14.6	13.3	6.7
Bornyl acetate (b.p. 223 $^{\circ}$ )	3.85	—	6.2	5.5	5.95	6.2	4.8

Table IV shows the relative retention volumes with respect to *d*-limonene of some oxygenated derivatives. The best degree of separation of these compounds was obtained on the Carbowax and APEG polyester column, and that of the former is compared in Fig. 3 with the separation obtained on silicone (Fig. 3(A)). Since Carbowax cannot be

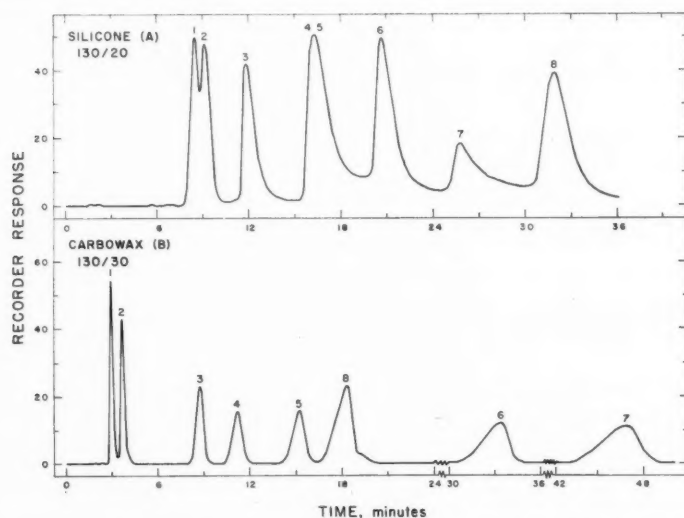


FIG. 3. Separation of terpenoid compounds on (A) silicone (at 130 $^{\circ}$  C and 30.0 ml helium per minute), (B) Carbowax (at 130 $^{\circ}$  C and 42.0 ml helium per minute).  
1, limonene; 2, 1,8-cineole; 3, fenchone; 4, citronellal; 5, camphor; 6,  $\alpha$ -terpineol; 7, citronellol; 8, bornyl acetate.

used above 100° to 120° C for long periods (8), the use of APEG polyester is to be preferred, especially so, since the latter has also a higher capacity (cf. Table II) and can be used for high boiling sesquiterpene alcohols and monophenols (see below) as well. All columns, except squalene, eluted *d*-limonene (b.p. 177° C) ahead of 1,8-cineole (b.p. 174° C) and all, except silicone and polyphenyl ether, eluted the higher boiling bornyl acetate ahead of  $\alpha$ -terpineol and citronellol. Bornyl acetate was eluted even ahead of camphor on the diglycerol column. Thus the use of different liquid phases can be used to differentiate between different functional groups (22). The sequence of separations on polyphenyl ether as compared with that obtained on the polyesters is noteworthy. From the present findings it is concluded that no single column will satisfy all requirements.

Silicone grease and the Craig polyesters (10) are known to be sufficiently stable at 160 to 220° C to allow the chromatography of compounds with higher boiling points than  $\alpha$ -terpineol. In addition, the polyphenyl ether was found to be suitable for runs at higher temperatures, and Table V shows the degree of separation of the closely related

TABLE V  
Relative retention times ( $\alpha$ -terpineol = 1) of sesquiterpene alcohols

Column (liquid phase)	Silicone	Polyphenyl ether	Polyesters		
			APEG	SEG	PEG
Temperature (° C)	160	160	190	190	190
Flow rate (ml He/min)	99	120	41.6	39.4	62.5
Inlet pressure (mm Hg)	2546	2546	1531	2029	2029
Retention time of $\alpha$ -terpineol	3.1	6.6	5.5	5.8	3.0
Occidentalol	4.9	4.6	3.4	3.0	3.0
Eudesmol a	6.5*	7.0*	5.25	5.1	4.5
Eudesmol b	—	—	5.4	5.3	4.7

\*Broad, unresolved peak.

sesquiterpene alcohols, occidentalol ( $C_{15}H_{24}O$ ) and eudesmol ( $C_{15}H_{26}O$ ), as compared with  $\alpha$ -terpineol obtained with these columns. Occidentalol differs structurally from eudesmol only by having one more double bond, yet it is completely separated from the latter even on the silicone column. This may, in part at least, be due to steric differences. The superior efficiency of the polyester columns is evident in that eudesmol is resolved partially into the  $\alpha$ - and  $\beta$ -isomers.

Since essential oils sometimes contain phenolic compounds, the degree of separation of the monophenols, anethole, eugenol, and isoeugenol, was tested on the APEG polyester and the polyphenyl ether columns. The former, at 190° C and 83.5 ml helium per minute, gave retention times of 5.3, 14.7, and 25.4 minutes, whereas the latter, at 220° C and 70.5 ml helium per minute, gave 4.3, 6.45, and 10.4 minutes respectively. Both columns gave even peaks without any sign of decomposition taking place. The separation of other types of phenols has been described by Janák *et al.* (23, 24).

#### CONCLUSIONS

1. Monoterpene hydrocarbons are best separated on columns using squalene, Carbowax 400, Craig polyesters, and polyphenyl ether as liquid phase at temperatures of 130° C and lower. At higher temperatures the polyester and polyphenyl ether columns give best results, separating oxygenated terpenes, sesquiterpene alcohols, and monophenols satisfactorily. The adipate polyethylene glycol (APEG) polyester column is most suited for all compounds tested.

2. The effect of temperature and sample size on the degree of separation is considerable, the lowest possible temperature giving best results from a qualitative and preparative point of view. With 6-mm diameter columns sample sizes above about 3  $\mu$ l cause considerable delays in the retention time of peak maxima as well as a broadening of peaks. The initial emergence of a peak is practically constant up to sample sizes which cause overloading of the columns. For qualitative work actual isolation of each component and determination of its physical properties is to be preferred over comparison of the retention time (or volume) with those of known compounds.

3. Chromosorb W, a calcined diatomaceous earth, was found to be a better solid support for the separation of terpenoid compounds than either washed Celite 545 or C-22 firebrick.

4. In preparative work with instruments using a thermal conductivity cell as detector, pure samples cannot be obtained with normal detector currents, and collection of thermally labile terpenes must be carried out in "blind" runs.

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## HYDROGENOLYSIS OF CARBOHYDRATES

### VIII. COMPARATIVE STUDIES ON METHYL GLUCOPYRANOSIDES<sup>1</sup>

P. A. J. GORIN

#### ABSTRACT

Several methyl glucopyranosides have been hydrogenated under pressure at 180° C with copper chromite catalyst in dioxane. Many glycosides underwent hydroxyl group inversion and another reaction observed consisted of hydrogenolytic removal of the methoxyl group coupled with reduction of a hydroxyl group to a methylene group. Other glycosides were stable under these conditions, and these included methyl  $\beta$ - and methyl  $\alpha$ -D-glucopyranosides and unexpectedly methyl  $\beta$ -D-mannopyranoside and methyl  $\alpha$ -D-talopyranoside. The data indicated that generally  $\beta$ -glycosides are more stable than their  $\alpha$ -anomers in the hexopyranoside series and that the methyl hexopyranosides are more stable than the methyl pentopyranosides. Explanations have been made in the theoretical section in order to cover these observations. At 240° C, however, methyl  $\alpha$ -D-glucopyranoside is hydrogenolyzed giving 11% of 1,5-anhydro-4-deoxy-hexitols. These polyols have been fractionated and the mixture shown to contain lyxo- and arabo-1,5-anhydro-4-deoxy-D-hexitols.

The earlier findings of von Rudloff, Bauer, and Stuetz (1) showed that the hydrogenolysis of methyl  $\alpha$ -D-glucopyranoside yields 1,5-anhydro-4-deoxy-hexitol (11% yield) along with many other products. The hydrogenolytic procedure was vigorous, the experiments being carried out with Adkins' copper chromite catalyst (2) at 240° C using dioxane as solvent under a hydrogen pressure of 170 atmospheres. More recent investigations (3, 4, 5, 6, 7) have indicated that at lower temperatures (180–220° C) some inversion of the asymmetric centers occurs as well as hydrogenolysis. However, methyl  $\alpha$ - and methyl  $\beta$ -D-glucopyranosides were found to be virtually unaffected at 180° C. Since the hydroxyl groups on methyl  $\beta$ -L-arabopyranoside are readily inverted by catalytic hydrogenation (3) the behavior of the methyl glucosides seemed anomalous. Therefore, another hexopyranoside methyl  $\alpha$ -D-mannopyranoside was hydrogenated at 180° C and was found to yield a mixture of isomeric glycosides.\* By fractionation, on a cellulose column (8), methyl  $\alpha$ -D-talopyranoside has been isolated from the mixture† together with unchanged methyl  $\alpha$ -D-mannopyranoside and a small amount of methyl  $\alpha$ -D-glucopyranoside. As the hydroxyl configurations in the substrate appeared to play a role in determining its susceptibility to hydrogenation other methyl  $\alpha$ -D-hexopyranosides were examined. Methyl  $\alpha$ -D-galacto- and -altro-pyranosides were transformed by hydrogenation to other isomers, mainly methyl  $\alpha$ -D-talopyranoside, which is a stable methyl glycoside under the conditions used (Table I). This was confirmed by synthesizing methyl  $\alpha$ -D-talopyranoside, hydrogenating it, and isolating the unchanged glycoside.

As well as the  $\alpha$ -glycosides, several methyl  $\beta$ -D-hexopyranosides were tested. These included methyl  $\beta$ -D-allo-, -altro-, -galacto-, -gluco-, and -manno-pyranosides (Table I) and as a group these compounds were more stable to hydrogenation than the  $\alpha$ -glycosides, a greater percentage of substrate being recovered unchanged. This stability was most pronounced in methyl  $\beta$ -D-gluco- and -manno-pyranosides which were virtually unaffected and were found to be the main end products of hydrogenation of the other  $\beta$ -glycosides.

In contrast to the hexopyranosides the methyl pentopyranosides, as represented by

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†This would appear to be a simple route by which to prepare methyl  $\alpha$ -D-talopyranoside.

TABLE I  
Products isolated from hydrogenation of methyl hexopyranosides at 180° C

Substrate	Product (% w/w)
Methyl $\alpha$ -D-glucopyranoside	98% Unchanged material
Methyl $\alpha$ -D-mannopyranoside	Methyl $\alpha$ -D-mannopyranoside (30%) Methyl $\alpha$ -D-talopyranoside (27%) Methyl $\alpha$ -D-glucopyranoside (3%)
Methyl $\alpha$ -D-galactopyranoside	Methyl $\alpha$ -D-glucopyranoside (33%) Methyl $\alpha$ -D-talopyranoside (9%) Polyols (7%) Methyl $\alpha$ -D-galactopyranoside (5%)
Methyl $\alpha$ -D-altropyranoside	Methyl $\alpha$ -D-talopyranoside (20%) Polyols (18%) Methyl $\alpha$ -D-mannopyranoside (11%)
Methyl $\alpha$ -D-talopyranoside	Mainly unchanged material
Methyl $\beta$ -D-glucopyranoside	Unchanged material
Methyl $\beta$ -D-mannopyranoside	87% Unchanged material
Methyl $\beta$ -D-galactopyranoside	Methyl $\beta$ -D-glucopyranoside (25%) Methyl $\beta$ -D-galactopyranoside (17.5%) Polyols (16%) Methyl $\beta$ -D-allopyranoside (3%)
Methyl $\beta$ -D-altropyranoside	Methyl $\beta$ -D-altropyranoside (24%) Polyols (16%) Methyl $\beta$ -D-mannopyranoside (15%)
Methyl $\beta$ -D-allopyranoside	Polyols (35%) Methyl $\beta$ -D-allopyranoside } 25% Methyl $\beta$ -D-glucopyranoside }

methyl  $\alpha$ -L-arabo- and -D-lyxo-pyranosides and methyl  $\beta$ -L-arabo- (cf. ref. 3), -D-ribo-, and -D-xylo-pyranosides, were much more prone to hydroxyl group inversion at 180° C (Table II). Acid hydrolysis of the product and detection of the free sugars by paper

TABLE II  
Products isolated from hydrogenation of methyl pentopyranosides at 180° C

Substrate	Product (% w/w)
Methyl $\alpha$ -L-arabopyranoside	Polyols (23%) Methyl $\beta$ -D-ribopyranoside (12%) Methyl $\alpha$ -L-lyxopyranoside (6%) Methyl $\beta$ -D-xylopyranoside (1%)
Methyl $\alpha$ -D-lyxopyranoside	Polyols (44%) Methyl ribopyranoside (?) Methyl arabopyranoside } 15% Methyl xylopyranoside } Methyl lyxopyranoside } Methyl $\alpha$ -D-lyxopyranoside (13%)
Methyl $\beta$ -L-arabopyranoside	Polyols (30%) Methyl $\beta$ -L-arabopyranoside (10%) Methyl $\alpha$ -D-xylopyranoside (5%)
Methyl $\beta$ -D-xylopyranoside	Polyols (29%) Methyl $\beta$ -D-ribopyranoside (17%) Methyl xylopyranoside } 12% Methyl arabopyranoside }
Methyl $\beta$ -D-ribopyranoside	Polyols (35%) Methyl ribopyranoside (16%) Methyl xylopyranoside } 7% Methyl lyxopyranoside } Methyl arabopyranoside }



chromatography indicated in each instance easy interconversion since two to four chemically different pentoses were present. Also, the pentopyranosides were hydrogenolyzed with greater ease to dihydroglycols (tetrahydropyrandiols) by reductive elimination of the methoxyl group coupled with reduction of a hydroxyl to a methylene group. The hydrogenation products of the methyl glycopyranosides are summarized in Tables I and II with the percentage of each compound contained in the reaction product as determined on column chromatographic separation.

It appears likely that resistance to catalytic hydroxyl inversion is affected by the shape of the substrate. For example, the 6-hydroxymethyl group seems to exert an influence in limiting hydroxyl group inversion and formation of compounds of the dihydroglycol type. The large substituent on C-5 would render the molecule more bulky and perhaps less flexible so that it could adopt fewer positions suited to reaction on the surface of the catalyst. Unfortunately too little is known about the surface properties of copper chromite to generalize on the probability of individual hydroxyls in the glycosides to invert. If, as has been assumed (7), inversion results from dehydrogenation followed by hydrogenation this ability would be concerned firstly, with the ease of dehydrogenation of the alcohol group to a ketone, and secondly with the specificity of reduction of the ketone to the two possible alcohols (Fig. 1). It has been shown that the rate of dehydrogenation

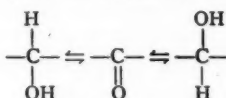


FIG. 1.

of a secondary alcohol with chromic acid in cyclohexane ring systems (9) to a ketone depends on the accessibility of the C-hydrogen atom (10) and not the rate of intermediate ester formation. The dehydrogenation rate was shown to be greater when the C-hydrogen atom was in the less sterically hindered equatorial position (9). However, this is in solution rather than on the surface of a catalyst. In order to explain the surprising observations that methyl  $\beta$ -D-mannopyranoside and methyl  $\alpha$ -D-talopyranoside are virtually unaffected under hydrogenation conditions it must be assumed that the catalyst plays a role in limiting dehydrogenation. This may well be because the surface contours of the copper chromite prevent the C-hydrogen atoms, some of which are equatorial (11), from becoming available. On the other hand, methyl  $\alpha$ - and  $\beta$ -D-glucopyranosides, which are also stable do not contain equatorial C-hydrogen atoms in their stable C-1 chair forms (11).

Since hydroxyl inversion readily occurs in polyhydroxyl compounds, even at temperatures as low as 180° C, it appeared likely that the syrupy 1,5-anhydro-4-deoxy-D-hexitol formed by hydrogenation of methyl  $\alpha$ -D-glucopyranoside at 240° C (1) was a mixture of stereoisomers and accordingly, this product has been examined further. Cellulose column chromatography of the syrupy polyols derived by catalytic deacetylation of the fractionated acetate contained two main components which were distinguishable on paper chromatograms. The fraction which was slower on paper was syrupy but gave a crystalline tris-*p*-nitrobenzoate derivative from which a crystalline polyol (I) of  $R_{\text{Rh}}$  1.1\* was regenerated. The 1,5-anhydro-4-deoxy-hexitol structure for the substance was indicated by carbon and hydrogen composition and its consumption of 1.0 molar equivalent of sodium periodate. If it is assumed that no inversion at C-5 takes place and that the six-membered ring is not modified in the course of hydrogenolysis the only

\*Throughout the text  $R_{\text{Rh}}$  denotes the distance moved by a spot on a paper chromatogram compared with rhamnose in the *n*-butanol-ethanol-water (40:11:19) v/v solvent.

alternative structure fitting the data is that of a dihydroglycol (IV). However, since periodic acid oxidation of I followed by sodium borohydride reduction gave an optically active triol (III) the dihydroglycol formula is invalidated since it would have given a triol (V) with no asymmetric centers (Fig. 2).

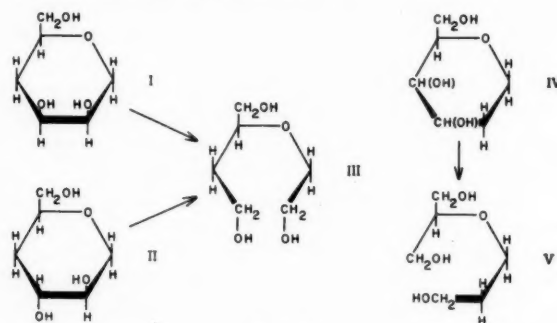


FIG. 2.

The other fraction having  $R_{\text{Rh}}$  1.3, from the cellulose column, also gave a crystalline tris-*p*-nitrobenzoate, which on debenzoylation yielded a syrupy polyol (II) which consumed 1.0 molar equivalent of sodium periodate. Periodic acid oxidation and sodium borohydride reduction of the resulting dialdehyde formed the same compound as obtained from I. Their identity was confirmed by comparison of their crystalline tris-*p*-nitrobenzoates.

Comparison of the rates at which I and II consumed lead tetraacetate showed that the former was oxidized 4 times faster in the initial stages. This difference which is appreciable considering that the  $\alpha$ -glycol groups are in a six-membered ring (4, 12, 13, 14) is interpreted as evidence that they are *cis* in I and *trans* in II. By consideration of the molecular rotations of various methyl hexopyranosides and 1,5-anhydro-hexitols theoretical values for the specific rotations of the four structural isomers of 1,5-anhydro-4-deoxy-D-hexitol can be calculated by use of Hudson's rules of optical superposition and isorotation (see Table III) (15). Since I has  $[\alpha]_{\text{D}} -50^\circ$  it is probably lyxo-1,5-anhydro-4-deoxy-D-hexitol and II ( $[\alpha]_{\text{D}} +19^\circ$ ) corresponds to arabo-1,5-anhydro-4-deoxy-D-hexitol. These compounds are different in hydroxyl configuration from methyl  $\alpha$ -D-glucopyranoside and it is likely that the other two possible stereoisomers are present in the hydrogenolysis product, but were not isolated through the limitations of the fractionation procedures. Although the 1,5-anhydro-4-deoxy-hexitols are difficult to distinguish chromatographically from the dihydroglycols of the hexose series, shown to be formed by hydrogenolysis under milder conditions (4), it seems unlikely that they are present, because they are extensively degraded by hydrogenolysis at  $220^\circ\text{C}$  (26).

The readiness of methyl glycopyranosides to form polyols on hydrogenolysis parallels their tendency to undergo hydroxyl inversion in the hexose as well as pentose series (except that with the hexoses a higher temperature is generally needed to remove the methoxyl group). For instance, methyl  $\beta$ -D-galactopyranoside is much more reactive at  $180^\circ\text{C}$  than methyl  $\alpha$ -D-glucopyranoside as far as hydroxyl group inversion is concerned. At  $200^\circ\text{C}$  the former is degraded to a mixture of dihydro-D-altral (12%), dihydro-D-glucal (31%), and dihydro-D-galactal (12%). But methyl  $\alpha$ -D-glucopyranoside is relatively inert at this temperature and complete hydrogenolysis only takes place at  $240^\circ\text{C}$ ,

TABLE III  
Calculated specific rotations of 1,5-anhydro-4-deoxy-D-hexitols

Polyols and calculated specific rotations	Reference compounds
ribo-1,5-Anhydro-4-deoxy-D-hexitol +46°	{ Methyl $\beta$ -D-allopyranoside ([M] <sub>D</sub> -9,510°) Methyl $\alpha$ -D-glucopyranoside (16) ([M] <sub>D</sub> +23,210°)
lyxo-1,5-Anhydro-4-deoxy-D-hexitol (I) -31°	{ Methyl $\alpha$ -D-talopyranoside ([M] <sub>D</sub> +4,070°) Methyl $\beta$ -D-mannopyranoside (17) ([M] <sub>D</sub> -13,390°)
-34°	{ 1,5-Anhydro-D-mannitol (18) ([M] <sub>D</sub> -8,360°) 1,5-Anhydro-D-talitol (19) ([M] <sub>D</sub> -1,800°)
xylo-1,5-Anhydro-4-deoxy-D-hexitol +106°	{ Methyl $\alpha$ -D-galactopyranoside (20) ([M] <sub>D</sub> +38,050°) Methyl $\beta$ -D-glucopyranoside (21) ([M] <sub>D</sub> -6,640°)
+67°	{ 1,5-Anhydro-D-glucitol (22) ([M] <sub>D</sub> +7,050°) 1,5-Anhydro-D-galactitol (23) ([M] <sub>D</sub> +12,790°)
arabo-1,5-Anhydro-4-deoxy-D-hexitol (II) +20°	{ Methyl $\alpha$ -D-altropyranoside (24) ([M] <sub>D</sub> +24,420°) Methyl $\beta$ -D-idopyranoside (25) ([M] <sub>D</sub> -18,430°)

to form the more stable 1,5-anhydro-4-deoxy-hexitols and degradation products such as ethylene and propylene glycols. Much of these lower molecular weight materials may therefore have been formed through an unstable 1,2-dihydroglycal intermediate rather than 1,5-anhydro-4-deoxy-D-hexitol which does not contain the 1,3-dihydroxy grouping which is susceptible to hydrogenolysis (27).

#### EXPERIMENTAL

Optical rotations were measured at 25° C. Evaporations were carried out under reduced pressure. The solvent used for paper chromatographic separations was *n*-butanol - ethanol - water (40:11:19 v/v). Reducing sugars were detected with the *p*-anisidine hydrochloride spray (28) and non-reducing sugars with ammoniacal silver nitrate (29). Acid hydrolysis of glycosides was carried out with *N* H<sub>2</sub>SO<sub>4</sub> at 100° C for 3 hours, the solutions neutralized with BaCO<sub>3</sub>, filtered, and evaporated.

##### A. Preparation of Reference Compounds

###### *Methyl $\beta$ -D-Allopyranoside*

D-Allose (500 mg), kindly supplied by Dr. A. C. Neish, was refluxed in 3% methanolic hydrogen chloride (20 ml) for 5 hours, and the solution neutralized, after it was cooled, with silver oxide which was then filtered off. The filtrate was evaporated to a syrup which crystallized and three recrystallizations from ethanol - ethyl acetate afforded material with m.p. 155-157° C and  $[\alpha]_D -49^\circ$  (*c*, 1.0, H<sub>2</sub>O), yield 95 mg. Calculated for C<sub>7</sub>H<sub>14</sub>O<sub>6</sub>: C, 43.3%; H, 7.3%. Found: C, 43.2%; H, 7.3%. The constants of the product agree with those given by Lindberg and Theander (30).

*Methyl  $\alpha$ -D-Talopyranoside and Derivative*

Syrupy D-talose (1.26 g) was heated for 4 hours in refluxing 3% methanolic hydrogen chloride (40 ml), the acid was neutralized ( $\text{Ag}_2\text{O}$ ), the solution filtered and evaporated to a syrup (1.17 g). Examination on a paper chromatogram indicated a main spot having  $R_{\text{Rh}}$  1.4 with a minor component of  $R_{\text{Rh}}$  1.1. The faster material was isolated by cellulose chromatography using benzene-ethanol-water (500:50:1 v/v) as the mobile phase. The product was a syrup (0.56 g) with  $[\alpha]_{\text{D}} +105^\circ$  (c, 1.0,  $\text{H}_2\text{O}$ ). Calculated for  $\text{C}_6\text{H}_{11}\text{O}_6 \cdot \text{OCH}_3$ :  $\text{OCH}_3$ , 16.0%. Found:  $\text{OCH}_3$ , 16.0%. The glycoside was designated the  $\alpha$ -configuration because of its strong dextrorotation.

The syrupy product (30 mg) was heated at  $100^\circ\text{C}$  for 2 hours in pyridine (0.5 ml) containing triphenylchloromethane (61 mg). After it was cooled, acetic anhydride (0.5 ml) was added and the solution left overnight. Then it was added to aqueous sodium bicarbonate and the insoluble material which formed was isolated and recrystallized twice from aqueous ethanol, then ethanol. The crystals (25 mg) had m.p.  $177\text{--}178^\circ\text{C}$  and  $[\alpha]_{\text{D}} +21^\circ$  (c, 1.3, pyridine) and analyzed for 2,3,4-tri-*O*-acetyl-6-*O*-triphenylmethyl methyl  $\alpha$ -D-talopyranoside. Calculated for  $\text{C}_{32}\text{H}_{34}\text{O}_9$ : C, 68.3%; H, 6.1%. Found: C, 68.2%; H, 6.2%.

*B. Hydrogenation of Methyl Glycopyranosides at  $180^\circ\text{C}$* 

In hydrogenation of the following methyl hexopyranosides identical procedures were used. The glycoside was added to one-third its weight of copper chromite in 50 parts of dioxane (v/w). The mixture was shaken at  $180^\circ\text{C}$  for 6 hours at a hydrogen pressure of 600 p.s.i. and after it was cooled the solution was filtered and evaporated. An attempt was then made to crystallize any sugars from solution and the resulting syrup was chromatographed on a cellulose column. The solvents for cellulose chromatography were benzene-ethanol-water (500:50:1 v/v) to isolate materials moving faster than rhamnose on a paper chromatogram. For compounds moving slower than rhamnose *n*-butanol one-quarter saturated with water was used.

When methyl pentopyranosides were hydrogenated the procedure was the same as above except for the relative proportion of components in the reaction mixture. In this case the weight of catalyst was 30% that of the methyl pentoside and the solvent used was 45 times that of the pentoside on a volume per unit weight basis.

(i) *Methyl  $\alpha$ -D-glucopyranoside*.—From the hydrogenation product of the glucoside (2.00 g) mainly unchanged material was recovered by crystallization from ethanol, m.p. and mixed m.p.  $165\text{--}166^\circ\text{C}$ . Column chromatography yielded only 42 mg of substance that ran at a different rate than methyl glucoside on a paper chromatogram.

(ii) *Methyl  $\beta$ -D-glucopyranoside*.—Using the same procedure as with the above  $\alpha$ -anomer only 9 mg of material was obtained not corresponding to methyl  $\beta$ -D-glucopyranoside. From ethyl acetate-ethanol the crystals had m.p. and mixed m.p.  $115\text{--}116^\circ\text{C}$ .

(iii) *Methyl  $\alpha$ -D-mannopyranoside*.—The mannoside (1.75 g) was hydrogenated and some unchanged glycoside (0.47 g) was recovered from the reaction mixture having m.p. and mixed m.p.  $192\text{--}195^\circ\text{C}$ . The remainder was fractionated on a cellulose column to give material containing methyl  $\alpha$ -D-talopyranoside (0.47 g) with  $[\alpha]_{\text{D}} +83^\circ$  (c, 3.3,  $\text{H}_2\text{O}$ ). Calculated for  $\text{C}_6\text{H}_{11}\text{O}_6 \cdot \text{OCH}_3$ :  $\text{OCH}_3$ , 16.0%. Found:  $\text{OCH}_3$ , 16.7%. Acid hydrolysis yielded a sugar which corresponded to talose and ran faster than galactose on a paper chromatogram, and which gave D-lyxohexose phenylosazone on treatment with aqueous phenylhydrazine acetate at  $80^\circ$  for 6 hours. The phenylosazone gave an X-ray diffraction pattern identical with authentic D-lyxohexose phenylosazone and different

from D-arabohexose, D-ribohexose, and L-xylohexose phenylosazones. The next fraction contained unchanged methyl  $\alpha$ -D-mannopyranoside (63 mg), m.p. and mixed m.p. 192–194° C. A later fraction (46 mg) from the column crystallized and two recrystallizations from ethanol – ethyl acetate yielded methyl  $\alpha$ -D-glucopyranoside, m.p. and mixed m.p. 167–168° C. Calculated for  $C_7H_{14}O_6$ : C, 43.3%; H, 7.3%. Found: C, 43.4%; H, 7.35%.

(iv) *Methyl  $\beta$ -D-mannopyranoside.*—Methyl  $\beta$ -D-mannopyranoside (1.16 g) on hydrogenation followed by acid hydrolysis yielded 137 mg of material from a cellulose column that did not correspond to mannose. In another experiment the unchanged glycoside was characterized as its tetraacetate, m.p. and mixed m.p. 161–163° C.

(v) *Methyl  $\alpha$ -D-galactopyranoside.*—Methyl  $\alpha$ -D-galactopyranoside (1.60 g) was hydrogenated and crystals were obtained from an ethanolic ethyl acetate solution of the product. The material (0.36 g) corresponded to methyl  $\alpha$ -D-glucopyranoside since it had m.p. and mixed m.p. 163–165° C and  $[\alpha]_D +161^\circ$  (*c*, 3.5,  $H_2O$ ). The mother liquor on cellulose chromatography gave three main fractions. These were a mixture (0.26 g) of polyols and methyl  $\alpha$ -D-talopyranoside having  $OCH_3$ , 9.3%, and  $[\alpha]_D +27^\circ$  (*c*, 1.2,  $H_2O$ ). The methoxyl content of the mixture corresponded to 58% of glycoside and it was acid hydrolyzed to give free aldose ( $R_F$  = talose) which was converted to D-lyxohexose phenylosazone by heating at 80° C for 6 hours with 4 moles of aqueous phenylhydrazine acetate. The identity of the phenylosazone was proved by its X-ray diffraction pattern, which was identical to that of an authentic specimen. The other two fractions which both crystallized from ethyl acetate – ethanol consisted of methyl  $\alpha$ -D-glucopyranoside (0.16 g), m.p. and mixed m.p. 165–166° C, and methyl  $\alpha$ -D-galactopyranoside (80 mg), m.p. and mixed m.p. 117–118° C.

(vi) *Methyl  $\beta$ -D-galactopyranoside.*—Hydrogenation of methyl  $\beta$ -D-galactopyranoside (2.0 g) gave a syrup from which methyl  $\beta$ -D-glucopyranoside (0.34 g), m.p. and mixed m.p. 116–117° C, was isolated. Cellulose chromatography gave as one of the main products a polyol fraction (0.32 g) and another contained glycosides (0.77 g) having  $R_{Rh}$  0.7. The latter was fractionated by crystallization from ethyl acetate – ethanol to give methyl  $\beta$ -D-glucopyranoside (163 mg) as thick prisms with m.p. and mixed m.p. 116–117° C and  $[\alpha]_D -37^\circ$  (*c*, 1.0,  $H_2O$ ) after two further recrystallizations. Calculated for  $C_7H_{14}O_6$ : C, 43.3%; H, 7.3%. Found: C, 43.2%; H, 7.5%. After the bulky prisms were removed a fluffy solid (62 mg) remained which on two recrystallizations from the same solvent yielded methyl  $\beta$ -D-allopyranoside with m.p. and mixed m.p. 157–158° C and  $[\alpha]_D -52^\circ$  (*c*, 1.6,  $H_2O$ ). Calculated for  $C_7H_{14}O_6$ : C, 43.3%; H, 7.3%. Found: C, 43.25%; H, 7.4%. The last fraction from the column consisted of unchanged methyl  $\beta$ -D-galactopyranoside (0.35 g) with m.p. and mixed m.p. 179–180° C.

(vii) *Methyl  $\alpha$ -D-altropyranoside.*—Methyl  $\alpha$ -D-altropyranoside (1.80 g) on hydrogenation gave a syrup which yielded crystals (0.19 g) from ethyl acetate – ethanol that corresponded to methyl  $\alpha$ -D-mannopyranoside with m.p. and mixed m.p. 191–193° C. Cellulose chromatography afforded three main fractions, the first of which (66 mg) appeared to be a polyol. The next fraction (0.13 g) afforded a sugar with  $R_{Rh}$  1.0 on hydrolysis which was not identified. The last portion of the column eluate gave a mixture (0.61 g) of polyol and methyl  $\alpha$ -D-talopyranoside which had  $OCH_3$  9.4% which indicated a glycoside content of 59%. Acid hydrolysis of the mixture afforded an aldose of  $R_F$  = talose which, on treatment with 4 moles of aqueous phenylhydrazine acetate at 80° C for 6 hours, gave D-lyxohexose phenylosazone identified by its X-ray diffraction pattern.

(viii) *Methyl  $\beta$ -D-altropyranoside.*—Cellulose chromatography of the hydrogenation product of methyl  $\beta$ -D-altropyranoside (1.04 g) afforded three fractions. The first was a



mixture of materials (164 mg) with mobility on a paper chromatogram greater than methyl  $\beta$ -altroside. The following fraction (253 mg) consisted of unchanged glycoside characterized as its tetraacetate, m.p. and mixed m.p. 98–99° C. Calculated for  $C_{14}H_{19}O_9 \cdot OCH_3$ :  $OCH_3$ , 8.35%. Found:  $OCH_3$ , 8.6%. The last material from the column was methyl  $\beta$ -D-mannopyranoside (155 mg), characterized as its tetraacetate, m.p. and mixed m.p. 161–163° C. Calculated for  $C_{18}H_{22}O_{10}$ : C, 49.7%; H, 6.1%. Found: C, 49.8%; H, 6.2%.

(ix) *Methyl  $\alpha$ -D-talopyranoside*.—Paper chromatography of the product (0.31 g) from hydrogenated methyl talopyranoside (0.34 g) indicated that the material was mainly unchanged taloside with  $R_{Rh}$  1.4. Only a trace of slower-moving material was detected. The product had  $OCH_3$  16.2% indicating that removal of the methoxyl group had not occurred. Acid hydrolysis of the product furnished an aldose, which on treatment with 1 mole of 1-methylphenylhydrazine (31) in refluxing ethanol gave crystals characterized as D-talose 1-methylphenylhydrazone, m.p. and mixed m.p. 150–152° C.

(x) *Methyl  $\beta$ -D-allopyranoside*.—Hydrogenation of the glycoside (0.48 g) yielded a syrup (0.36 g) which on cellulose chromatography was found to consist of 0.17 g of materials with  $R_{Rh} > 1.0$  on a paper chromatogram and 122 mg of a mixture of methyl  $\beta$ -D-allo- and -gluco-pyranosides. Fractional crystallization from ethyl acetate–ethanol gave 19 mg of the former with m.p. and mixed m.p. 154–156° C and 29 mg of the latter which had m.p. and mixed m.p. 115–116° C.

(xi) *Methyl  $\alpha$ -L-arabopyranoside*.—The glycoside (2.22 g) was hydrogenated and the resulting mixture chromatographed on cellulose. The first fraction consisted of polyols (0.50 g) and tosylation of the mixture (14) gave a product which was fractionally crystallized to yield ditosyl-*trans*-tetrahydropyrandiol, m.p. and mixed m.p. 157–161° C, and ditosyl-*cis*-tetrahydropyrandiol, m.p. 125–129° C. A second fraction (0.26 g),  $[\alpha]_D -98^\circ$  (c, 1.0,  $H_2O$ ), from the column crystallized to give methyl  $\beta$ -D-ribopyranoside from Skelly "F"-ethyl acetate, m.p. and mixed m.p. 83–84° C. The next material eluted (0.13 g) was shown to be methyl  $\alpha$ -L-lyxopyranoside, m.p. 109–110° C and  $[\alpha]_D -57^\circ$  (c, 1.0,  $H_2O$ ), after two recrystallizations from ethyl acetate–ethanol, which gave an X-ray diffraction pattern identical with that of the D-isomer. Calculated for  $C_6H_{12}O_5$ : C, 43.9%; H, 7.4%. Found: C, 44.1%; H, 7.4%. The last fraction from the column weighed 0.16 g and from this 16 mg of methyl  $\beta$ -D-xylopyranoside, m.p. and mixed m.p. 159–161° C, was obtained after two recrystallizations from ethanol–ethyl acetate.

(xii) *Methyl  $\beta$ -L-arabopyranoside*.—The hydrogenolysis product from methyl  $\beta$ -L-arabopyranoside (2.22 g) was very complex and acid hydrolysis showed that it contained all four chemically different pentosides. On cellulose chromatography a polyol fraction (0.66 g) was obtained corresponding to the two possible tetrahydropyrandiols. Very little further fractionation was obtained although methyl  $\beta$ -L-arabopyranoside (0.22 g), m.p. and mixed m.p. 167–168° C, was crystallized from ethanol and later 109 mg of a syrupy glycoside, with  $[\alpha]_D +128^\circ$  (c, 2.2,  $H_2O$ ) which gave xylose on acid hydrolysis, was obtained. Although the latter product did not crystallize it appears that it was methyl  $\alpha$ -D-xylopyranoside.

(xiii) *Methyl  $\alpha$ -D-lyxopyranoside*.—The glycoside (2.22 g) was hydrogenated and on cellulose chromatography three fractions were obtained. A considerable proportion of tetrahydropyrandiols (0.97 g) was shown to be present. In this fraction it appeared that some methyl riboside was present since ribose was obtained on a paper chromatogram by hydrolyzing the syrup with acid. The next fraction (0.29 g) contained methyl  $\alpha$ -D-lyxopyranoside, m.p. and mixed m.p. 107–109° C and the last portion (0.33 g) from

the column was shown to contain xyloside, arabinoside, and lyxoside by acid hydrolysis followed by paper chromatography.

(xiv) *Methyl  $\beta$ -D-ribopyranoside*.—When methyl  $\beta$ -D-ribopyranoside (2.20 g) was hydrogenolyzed and the product chromatographed on cellulose a considerable proportion of polyol (1.11 g) was found. The polyol had  $\text{OCH}_2$  6.3% and on acid hydrolysis some ribose was formed, which indicates that 31% of the mixture consisted of methyl riboside. The remainder of the column eluate (0.16 g) consisted of a mixture of xyloside, riboside, and arabinoside as shown by paper chromatography of the acid hydrolyzate.

(xv) *Methyl  $\beta$ -D-xylopyranoside*.—The xyloside (1.11 g) was hydrogenolyzed and chromatographed on cellulose in the usual way. The initial fraction appeared to be tetrahydropyrandiols (0.32 g) and later portions were obtained which consisted of methyl- $\beta$ -D-ribopyranoside (m.p. and mixed m.p. 80–81° C; 0.19 g) from ethyl acetate – Skelly F, and a xyloside (0.13 g) which could not be crystallized but which gave xylose on acid hydrolysis.

### C. Hydrogenation of Glycosides at Temperatures > 180° C

#### *1,5-Anhydro-4-deoxy-D-hexitols from Hydrogenolysis of Methyl $\alpha$ -D-glucopyranoside at 240° C*

The hydrogenolysis of methyl  $\alpha$ -D-glucopyranoside at 240° C was described by von Rudloff, Bauer, and Stuetz, who acetylated the product and fractionally distilled the acetates (1). Their still residue contained acetates of the 1,5-anhydro-4-deoxy-D-hexitols and this (7.32 g) was deacetylated with 0.1 mole of sodium methoxide in methanol (150 ml) for 3 hours. The polyols (4.92 g) obtained on evaporation consisted of two main fractions of  $R_{\text{Rh}}$  1.1 and 1.3. Cellulose chromatography gave a syrup (1.81 g) consisting of mainly the former and this was heated at 80° C for 1 hour with *p*-nitrobenzoyl chloride (13 g) in pyridine (30 cc). The solution was poured into excess aqueous sodium bicarbonate and after 30 minutes stirring the precipitate was collected, washed with water, and dried. Three recrystallizations from ethyl acetate – Skelly F brought the tris-*p*-nitrobenzoate (4.84 g) to a constant m.p. of 113–115° C; it had  $[\alpha]_{\text{D}} -83^\circ$  (*c*, 1.1,  $\text{CHCl}_3$ ). Calculated for  $\text{C}_{27}\text{H}_{21}\text{O}_{13}\text{N}_3$ : C, 54.6%; H, 3.6%. Found: C, 54.7%; H, 3.3%. Debenzoylation of the product (4.8 g) with 0.1 mole of sodium for 1 hour in boiling methanol (200 cc), followed by evaporation and deionization yielded crystals which were recrystallized twice from ethyl acetate – methanol. Yield, 0.37 g. The 1,5-anhydro-4-deoxy-D-hexitol corresponded to the fraction having  $R_{\text{Rh}}$  1.1 and had m.p. 80–81° C,  $[\alpha]_{\text{D}} -50^\circ$  (*c*, 0.8,  $\text{H}_2\text{O}$ ) and consumed 1.0 mole of aqueous sodium periodate overnight. Calculated for  $\text{C}_6\text{H}_{12}\text{O}_4$ : C, 48.6%; H, 8.2%. Found: C, 48.7%; H, 8.2%.

The polyol having  $R_{\text{Rh}}$  1.3 was eluted later from the cellulose column and it (1.08 g) gave a tris-*p*-nitrobenzoate having m.p. 115–119° C and  $[\alpha]_{\text{D}} +59^\circ$  (*c*, 1.1,  $\text{CHCl}_3$ ). Calculated for  $\text{C}_{27}\text{H}_{21}\text{O}_{13}\text{N}_3$ : C, 54.6%; H, 3.6%. Found: C, 54.5%; H, 3.9%. Catalytic debenzylation furnished a syrupy 1,5-anhydro-4-deoxy-D-hexitol with  $R_{\text{Rh}}$  1.3 and  $[\alpha]_{\text{D}} +19^\circ$  (*c*, 1.1,  $\text{H}_2\text{O}$ ), which consumed 1.0 mole of aqueous sodium periodate in 18 hours.

#### *Structure of the 1,5-Anhydro-4-deoxy-D-hexitols*

The anhydro deoxyhexitol of  $R_{\text{Rh}}$  1.1 (150 mg) was oxidized with 0.1 *M* periodic acid (1.5 moles) for 18 hours, the solution neutralized ( $\text{BaCO}_3$ ) and filtered into an aqueous solution (10 ml) of sodium borohydride (100 mg). After 30 minutes the solution was acidified with acetic acid, treated with Amberlite IR-120, filtered, and evaporated to a

crust which was repeatedly dissolved in methanol which was then evaporated. The syrupy polyol (132 mg) had  $[\alpha]_D -20^\circ$  (*c*, 2.0, H<sub>2</sub>O) and 75 mg of it was *p*-nitrobenzoylated in a manner similar to that described above to yield after three recrystallizations from ethyl acetate – pentane a tris-*p*-nitrobenzoate with m.p. 103–104° C and  $[\alpha]_D -26^\circ$  (*c*, 2.3, CHCl<sub>3</sub>). Calculated for C<sub>27</sub>H<sub>23</sub>O<sub>13</sub>N<sub>3</sub>: C, 54.3%; H, 3.9%. Found: C, 54.3%; H, 3.9%.

Similar treatment of the anhydro deoxyhexitol of *R*<sub>Rh</sub> 1.3 (60 mg) with periodic acid and sodium borohydride gave the open chain polyol with  $[\alpha]_D -16^\circ$  (*c*, 1.0, H<sub>2</sub>O) from which gave an identical tris-*p*-nitrobenzoate, m.p. 98–102° and  $[\alpha]_D -22^\circ$  (*c*, 1.4, CHCl<sub>3</sub>) was prepared. It had an X-ray crystal diagram similar to that of the *p*-nitrobenzoate obtained from the triol of *R*<sub>Rh</sub> 1.1. Calculated for C<sub>27</sub>H<sub>23</sub>O<sub>13</sub>N<sub>3</sub>: C, 54.3%; H, 3.9%. Found: C, 54.5%; H, 3.9%.

Twenty-five milligrams of each 1,5-anhydro-4-deoxy-hexitol was dissolved in water (0.3 ml) and acetic acid (10 ml). A 1% solution of lead tetraacetate in acetic acid (10 ml) was added, the consumption of oxidant followed and the following values obtained:

Time (minutes)	10	35	70	135	205
Material of <i>R</i> <sub>Rh</sub> 1.1, uptake in moles/mole	0.26	0.62	0.79	0.89	0.88
Material of <i>R</i> <sub>Rh</sub> 1.3, uptake in moles/mole	0.07	0.16	0.25	0.30	0.34

#### *Hydrogenolysis of Methyl β-D-galactopyranoside at 200° C*

Methyl β-D-galactopyranoside (2.00 g) was hydrogenolyzed at 200° C using the proportions described previously. Paper chromatographic examination of the product indicated that all the starting material had been destroyed. In order to decompose any deoxy glycosides that may have been formed in the reaction, the product was heated for 18 hours at 100° C in *N* H<sub>2</sub>SO<sub>4</sub>. The solution was then neutralized (BaCO<sub>3</sub>), filtered, and evaporated to a syrup (1.56 g), 0.69 g of which was fractionated on a cellulose column using benzene-ethanol-water (500:50:1 v/v) as solvent. From the column, dihydro-D-altral (80 mg), m.p. 105–106° C, dihydro-D-glucal (213 mg), m.p. 75–76° C, and dihydro-D-galactal (82 mg), m.p. 130–132° C, were obtained. All the above melting points were undepressed on admixture of the crystals with authentic specimens.

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## THE ENERGY OF HYDROGEN BONDING IN THE SYSTEM: ACETONE-CHLOROFORM

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### ABSTRACT

It is shown that

- (1) acetone and chloroform form a compound stable in the solid state;
- (2) acetone and carbon tetrachloride do not form a compound;
- (3) the enthalpies of mixing of acetone and chloroform and of acetone and carbon tetrachloride have been determined;
- (4) from these figures the energy of hydrogen bonding in the acetone-chloroform system is evaluated as  $2.7 \text{ kcal} \pm 0.1$ .

The authors are engaged in a general investigation, including heats of mixing, of the ternary system: acetone-benzene-chloroform. It was pointed out to us, by Dr. W. Schneider of the National Research Council of Canada, that the data obtained would, with slight extension, enable us to determine the energy of formation of the linkage in the compound



The existence of a compound,  $(\text{CH}_3)_2\text{CO} \cdot \text{CHCl}_3$ , has been long suspected. Indeed, Dolezalek (1) thought that he had proved the existence of this compound by an argument which would not now be considered completely acceptable. Nevertheless, the palpable evolution of heat when acetone and chloroform are mixed indicates, at least, that something of the nature of compound formation is taking place. It was therefore necessary, first, to demonstrate that acetone and chloroform do form a molecular compound and then to determine the enthalpies of mixing of acetone with carbon tetrachloride. Finally, it had to be shown that acetone and carbon tetrachloride do not form a compound as, indeed, from the nature of their formulae, is hardly likely.

### EXPERIMENTAL

The existence of a compound was demonstrated by a study of the freezing-point diagram. A copper-constantan thermocouple and a Brown recorder were used; liquid nitrogen was the cooling agent. The mixture was placed in a double-jacketed vessel. The degree of vacuum in the jacket could be varied to produce any desired rate of cooling. All mixtures were stirred vigorously. The reagents were of highest purity and were distilled. The thermocouple was calibrated with acetone, chloroform, and mercury, whose freezing points were taken as  $-95^\circ \text{C}$ ,  $-63.5^\circ \text{C}$ , and  $-38.87^\circ \text{C}$  respectively.

The same technique was employed in the investigation of the system acetone-carbon tetrachloride, except that the very small heat of fusion of carbon tetrachloride (4.16 cal per gram) made thermal analysis an insensitive method, for mixtures containing large amounts of carbon tetrachloride. Hence, when dealing with such mixtures, where no appreciable halt or point of inflection could be detected on the cooling curve, the partially

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frozen mixtures were allowed to heat up slowly, with vigorous stirring and the temperature of disappearance of the last crystals noted. This, admittedly, tends to give high results. Mixtures richer in acetone showed both primary freezing and eutectic halt, without any difficulty.

Heats of mixing were determined by having a weighed amount of one liquid in a magnetically stirred vacuum-walled calorimeter and the second liquid, also weighed, in a second such vessel. One set of junctions of a 20-junction copper-constantan thermopile was in the calorimeter and the other set was in the other vessel, so that the thermopile measured the difference in temperature of the two; allowance was made for any slight original difference in temperature. The thermopile had a sensitivity of about  $0.2^{\circ}\text{C}$ , corresponding to the minimum reading of the recorder chart. A suitable quantity of the second liquid was forced through a coarse capillary into the calorimeter, the amount being obtained by weighing at the end of the experiment. The average rise in temperature was about  $7^{\circ}$ . The mixing of acetone and carbon tetrachloride is an endothermal process and here the fall in temperature is much less. The usual method of radiation correction was applied and the water equivalent of calorimeter and contents was determined electrically, for each individual experiment. Current through the immersed platinum heating coil was determined from the voltage drop over a standard resistance. By this method, temperatures are not measured as such; the electrical input is multiplied by the ratio of two vertical lines on the recorder graph.

## RESULTS

TABLE I  
Freezing points of the system: acetone-chloroform

Mole % acetone	F.p. in $^{\circ}\text{C}$	Eutectic halt
9.8	-72	-108
20.2	-80	-107
20.5	-81	-108
29.8	-93	-107
30.9	-103	-108
34.2	Eutectic	-108.5
34.8	-107	—
40.2	-106.5	-108.5
45.1	-106	-107.5
49.9	-106	—
50.1	-106	—
55.1	-107	—
60.3	-108	—
65.4	-110	—
69.2	-112	—
70.0	-112	—
77.3	-110	-115
90.0	-99	—

When the above results are plotted, a three-branch curve with an extremely flat maximum at 50 mole % composition is obtained. This indicates that the compound  $(\text{CH}_3)_2\text{CO} \cdot \text{CHCl}_3$  exists in the solid state but that it is highly dissociated in the molten state. The melting point of the compound is  $-106^{\circ}\text{C}$  and the two eutectics lie at  $-108^{\circ}$  (31 mole % acetone) and  $-115^{\circ}$  (74 mole % acetone).

When the above figures are plotted a simple two-branch curve results, with a eutectic

TABLE II  
Freezing points of the system: acetone - carbon tetrachloride

Mole % acetone	F.p. in °C	Eutectic halt
12.7	-39	—
24.6	-51	—
36.0	-55.5	—
41.4	-58	—
46.8	-61.5	—
50.0	-65	—
56.8	-68	—
66.3	-75	—
83.9	-95	-105
92.3	-102	-105

lying at 87.5 mole % acetone and at  $-105^{\circ}\text{C}$ . Hence acetone and carbon tetrachloride do not form a compound.

The enthalpies of mixing of acetone and chloroform have been determined by Hirobe (5), by an ingenious and apparently accurate method. Our results are given in Table III.

Wyatt (2), from a study of the freezing-point diagram, finds a 1:1 compound of acetone and chloroform, melting congruently at  $-99.5^{\circ}\text{C}$ , the two eutectics lying at  $-117^{\circ}$  (73 mole % acetone) and  $-114^{\circ}$  (38 mole % acetone). Wyatt (3) also claims the existence of a 1:1 compound of acetone and carbon tetrachloride, melting incongruently, with a peritectic at  $-75.5^{\circ}$ , and a eutectic at  $-101^{\circ}$ , and 8.5 mole % carbon tetrachloride. Our figures for the eutectic temperature and composition are in fair agreement with those of Wyatt and our figures do not disprove Wyatt's statement of an allotropic transformation of carbon tetrachloride at  $-48^{\circ}$ . Timmermans (4), however, is unable to find this compound.

On the face of it, the formation of a compound does not seem very likely, since the enthalpy of mixing is positive. For the system, acetone-chloroform, where a compound definitely exists, the enthalpy is strongly negative.

TABLE III  
Enthalpies of mixing of acetone and chloroform

Mole % chloroform	$\Delta H$ in gram calories per mole mixture	$\Delta H$ in gram calories per mole acetone
5.9	-68.3	-72
15.7	-174.2	-206
30.3	-328.1	-471
40.6	-399.7	-673
48.2	-434.1	-838
51.0	-449.7	-918
59.3	-465.9	-1145
70.7	-441.9	-1505
78.2	-362.6	-1664
88.0	-223.3	-1861
93.6	-126.1	-1970

When the above results are plotted along with those of Hirobe, the agreement is seen to be rather close. Our maximum occurs at 59.3 mole % chloroform and  $\Delta H = -465.9$ , while Hirobe's maximum occurs at 54.8 mole % chloroform and  $\Delta H = -471.5$ .

TABLE IV  
Enthalpies of mixing of acetone and carbon tetrachloride

Mole % carbon tetrachloride	$\Delta H$ in gram calories per mole of mixture	$\Delta H$ in gram calories per mole acetone
4.9	6.5	6.8
9.4	5.1	5.6
17.1	11.6	14.0
31.7	16.2	23.7
41.4	30.7	52.0
42.1	30.8	53.2
49.0	40.5	79.4
49.7	45.2	90.0
51.1	50.0	102
62.5	57.0	152
67.6	55.0	170
74.4	55.4	216
74.7	54.8	217
78.9	48.9	232
88.1	41.8	351
92.8	32.9	457

The only reference in the literature to the enthalpy of mixing of acetone and carbon tetrachloride is by Timofeev (6), who gives  $Q = -1.7$  kilojoule per mole solute (heat absorbed). The dilution is not stated. The graph of our results exhibits a very flat maximum at about 65 mole % carbon tetrachloride and  $\Delta H = 57.0$  cal per mole mixture.

#### DISCUSSION

Acetone and chloroform form a compound,  $(\text{CH}_3)_2\text{CO} \cdot \text{CHCl}_3$ , stable in the solid state though highly dissociated in the molten state. In agreement with this, the enthalpy of mixing is negative. Acetone and carbon tetrachloride form no such compound and the enthalpy of mixing is small and positive. This is what would be expected of an ideal mixture (no appreciable interaction other than dilution). Although the compound of acetone and chloroform is highly dissociated in the liquid state, presumably the dissociation will be reduced to zero in the presence of an infinite excess of either chloroform or acetone. It is for this reason that we have evaluated the enthalpies of mixing per mole of acetone. When these values are extrapolated to 100 mole % chloroform (infinite excess per mole of acetone), we obtain, for the acetone-chloroform system,  $\Delta H = -2090$  calories, and for the acetone-carbon tetrachloride system,  $\Delta H = +625$  calories. We therefore deduce the enthalpy of formation of the compound (energy of hydrogen bonding) to be  $-2090 - 625 = -2715$  calories, say  $2.7 \pm 0.1$  kcal, since the calculation of  $\Delta H$  for small percentages of acetone involves multiplication by a large factor (say 15) with consequent magnification of experimental error. The form of the graph, however, rules out extreme error, so that the value given for the hydrogen bond is correct to the limits given.

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**A CHROMATOGRAPHIC ANALYSIS OF THE PRODUCT FROM THE  
TRITOSYLATION OF SUCROSE:  
CRYSTALLINE 6,6'-DI-O-TOSYLSUCROSE<sup>1</sup>**

R. U. LEMIEUX AND J. P. BARRETTE

ABSTRACT

Chromatographic analysis on silicic acid of the so-called "tri-*O*-tosylsucrose" which is formed in 95% yield on the reaction of 3 moles of *p*-toluenesulphonyl chloride with 1 mole of sucrose in pyridine at 0° has shown the substance to contain penta-, tetra-, tri-, and di-*O*-tosylsucroses in the molar ratios 0.05:0.33:1:1, respectively. Any mono-*O*-tosylsucrose present in the reaction mixture may have been lost in the isolation of the product. The composition of the product was substantially the same when the reaction was performed at -18°. The chromatogram separated the tritosylates into two subfractions. The major subfraction represented 29% by weight of the original "tri-*O*-tosylsucrose" and could be converted to 1',2:3,6:3',6'-trianhydrosucrose in 77.4% yield. Therefore, the so-called "tri-*O*-tosylsucrose" can contain only 25-29% of 1',6,6'-tri-*O*-tosylsucrose. 6,6'-Di-*O*-tosylsucrose crystallized from the di-*O*-tosylsucrose fraction in 10% over-all yield.

Compton (1) obtained evidence that primary hydroxyl groups can undergo tosylation substantially more rapidly than do the secondary positions in a carbohydrate structure. He obtained yields of 41% and 36% of the 6-*O*-tosyl derivatives on monotosylations of the methyl  $\beta$ - and  $\alpha$ -D-glucopyranosides, respectively. These results indicate a difference in reactivity between the primary position and the average secondary position in these compounds in the order of 7. On the other hand, Hockett and Downing (2) found that the hydroxyl groups in 1,2:5,6-di-*O*-isopropylidene- $\alpha$ -D-glucose and 1,2:3,4-di-*O*-isopropylidene- $\alpha$ -D-galactose differed in reactivity by a factor of 70. Little is known about the factors responsible for such differences in reactivity. Undoubtedly, non-bonded interactions in the transition state are important and probably mainly responsible for the generally greater reactivity of primary positions (3, 4). It should be noted, for example, that the large difference in reactivity found for the di-*O*-isopropylidene derivatives of glucose and galactose may be mainly due to the fact that the 3-hydroxyl group of the glucose derivative is eclipsed with the 4-position. Lemieux and McInnes (5) have recently shown that intramolecular hydrogen bonding also can strongly influence the rate of reaction. Furthermore, little information is available on the relative rates for the tosylation of the starting material and the first product of tosylation. Experience in related fields has shown (6, 7, 8) that this can be a dominant feature of the esterification of polyhydroxy compounds with hydrophobic reagents. Thus, when it is considered that the reactivities of both the primary and the secondary hydroxyl groups must vary considerably amongst themselves, it seems clear that attempts at preferential tosylation of the primary positions of polyhydroxy compounds can be expected to proceed in widely varying yields.

Hockett and Zief reported the preparation (9) of a substance termed "tritosylsucrose" by treatment of 1 mole of sucrose with 3 moles of tosyl chloride in pyridine at 0°. The product was not well characterized; nevertheless, it was suggested that the compound was probably "almost entirely" substituted at the three primary positions. The product is in fact highly substituted at the 6- and 6'-positions, since reaction with sodium iodide in acetone (10, 11, 12) affords material containing two iodine atoms per tosyl group. Lemieux and Barrette (13) have shown that the 1'-tosyloxy group of 1',4,6'-tri-*O*-tosyl-

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sucrose pentaacetate is not replaced by iodine when treated with sodium iodide in acetone. Since no information was gained regarding the nature of the third tosyloxy group of the so-called "tri-*O*-tosylsucrose" and since the substance is amorphous, the results shedded no light on either the extent of substitution at the 1'-position or the distribution of the tosyl groups among the sucrose residues. The so-called "tri-*O*-tosylsucrose" was obtained in yields above 95% and analyzed well for a sucrose tritosylate. Consequently, it can be assumed that there is no appreciable tendency for a pile-up of tosyl groups on relatively few sucrose molecules. Bragg and Jones (12) have made a study of the so-called "tri-*O*-tosylsucrose" by methylation, followed by reductive detosylation and hydrolysis, and inspection of the partially methylated D-glucose and D-fructose derivatives thus formed. Inspection of their results reveals no basis for the contention that the substance "consisted mainly therefore of 6,1',6'-tri-*O*-tosylsucrose". The present authors entertained considerable doubt as to this characterization first of all in view of ordinary kinetic considerations and also in view of the low yield (3.5%) of 1',2:3,6:3',6'-trianhydrosucrose which was isolated (13, 14) on alkaline alcoholysis of the substance. It was believed of real interest to obtain a proper characterization of the substance in order the better to orientate our thinking and to justify our suspicions of previous interpretations of experimental results related to this problem. Our approach was to analyze the so-called "tri-*O*-tosylsucrose" by chromatography on silicic acid columns, a procedure which Jeanloz (15) has shown to be of great value for the separation of certain carbohydrate derivatives.

"Tri-*O*-tosylsucrose" was prepared by the method of Hockett and Zief (9) both at 0° and at -18°. The amorphous products were chromatographed on paper impregnated with silicic acid (16), using diisobutyl ketone:acetic acid:water (40:25:5) as solvent. The zones were located by dipping the paper in an aqueous solution of Rhodamine 6G (16). Fluorescent spots were observed under ultraviolet light at  $R_f$  values of 0.15, 0.40, 0.65, and 0.90. It was established that these corresponded to zones of di-, tri-, tetra-, and penta-*O*-tosylsucrose, respectively, by the chromatography of the components isolated by column chromatography on silicic acid using the same solvent system. This paper chromatographic technique proved extremely useful for a rapid preliminary inspection of a product and the establishment of an appropriate solvent system for the column chromatography.

The column chromatograms allowed the isolation of fractions that require the "tri-*O*-tosylsucrose" prepared at 0° to be, chemically, a highly heterogeneous substance containing penta-, tetra-, tri-, and di-*O*-tosylsucroses in the molar ratios 0.05:0.33:1:1, respectively (see Table I).

TABLE I  
Chromatography of "sucrose tritosylates"

	Penta- <i>O</i> - tosyl- sucrose	Tetra- <i>O</i> - tosyl- sucrose	Tri- <i>O</i> -tosylsucrose		Di- <i>O</i> -tosylsucrose	
			Fraction A	Fraction B	Fraction C*	Fraction D
Color of fluorescence	Red	Pink	Yellow	Pink	Yellow	Yellow
Tube No.	17-22	24-34	39-57	58-62	93-105	86-110
Weight of material (g)	0.18	1.53	2.65	1.17	0.92	2.11
Per cent of mixture (w/w)	2.0	17.0	29.0	13.0	10.0	24.0
Sulphur content (%)						
Found:	13.90	13.40	11.84	11.41	10.12	9.22
Calc.:	14.4	13.38	11.93	11.93	9.85	9.85
[ $\alpha$ ] <sub>D</sub> (chloroform)	+42.3	+35.0	+37.5	+33.0	+54.0	+35.0

NOTE: The material, 9.05 g, was prepared at 0°.

\*Crystalline 6,6'-di-*O*-tosylsucrose.



The tri-*O*-tosylsucrose fraction could be resolved into two subfractions which comprised 29.0% (tri-*O*-tosylsucrose A) and 13.0% (tri-*O*-tosylsucrose B) by weight of the original "tri-*O*-tosylsucrose". Both these fractions have thus far resisted crystallization. Their sulphur contents were in good agreement with that expected for sucrose tritosylates. That the substances were in fact different was obvious from the following properties. Whereas the A fraction gave a yellow fluorescence with Rhodamine 6G, and readily consumed 2.82 moles of periodate per mole, the B fraction produced a pink fluorescence and consumed only 1.75 moles of periodate per mole. Furthermore, the A and B fractions underwent replacement of 1.87 and 1.63 tosyloxy groups when treated with sodium iodide in acetone. These results clearly indicate that both fractions are mixtures of tritosylated sucroses. However, the high periodate consumption by the A fraction shows that it must be mainly (about 78%) 1',6,6'-tri-*O*-tosylsucrose. This conclusion was substantiated by the formation of 1',2:3,6:3',6'-trianhydrosucrose (13) in 77.4% yield on treatment of the A fraction with sodium methoxide in methanol. These results provide unequivocal evidence that the trianhydrosucrose in fact arises from 1',6,6'-tri-*O*-tosylsucrose (14).

The di-*O*-tosylsucrose fraction deposited a 10% over-all yield (by weight) of crystalline compound (fraction C), m.p. 108–110°,  $[\alpha]_D +54^\circ$  in ethanol. The sulphur content corresponded to that expected for di-*O*-tosylsucrose and the compound only reduced Fehling's solution after acid hydrolysis. The compound was acetylated and the acetyl derivative, on treating with sodium iodide in acetone at 100°, produced a substance with the iodine content expected for a diiododideoxysucrose hexaacetate. Also, the nuclear magnetic resonance spectrum of the diiodo compound was devoid of the signals characteristic for the tosyl group. These properties require that the compound be 6,6'-di-*O*-tosylsucrose. The syrup (fraction D) which remained after crystallization of the 6,6'-di-*O*-tosylsucrose had a sulphur content close to that expected for a sucrose ditosylate (see Table I). Treatment of the hexaacetate derivative with sodium iodide in acetone replaced only 1.10 of the tosyloxy groups. This result shows that the 1'-hydroxyl group and perhaps certain secondary groups can compete favorably with the 6- or 6'-hydroxyl groups, or both in the tosylation reaction. It will be seen later on that the competition is undoubtedly mainly from the 1'-position and that, consequently, the di-*O*-tosylsucrose fractions (C and D combined) may be almost entirely composed of not greatly different amounts of the 1',6-, 1',6'-, and 6,6'-di-*O*-tosylsucroses.

The substances isolated from the other two bands of the chromatogram possessed sulphur contents in good agreement with those expected for tetra- and penta-*O*-tosylsucroses. The results of the chromatogram are listed in Table I and the course of the tosylation is described in Fig. 1.

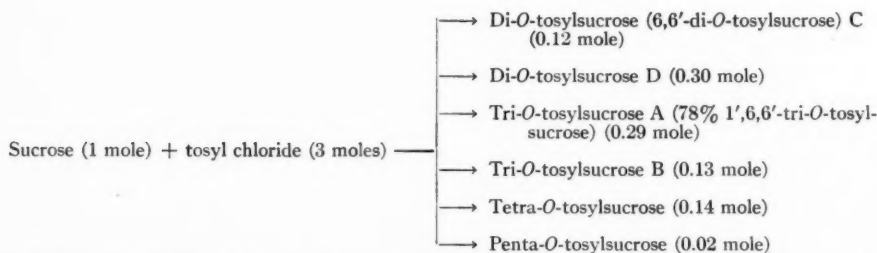


FIG. 1. Distribution of the tosylated sucroses formed in the reaction of 1 mole of sucrose with 3 moles of tosyl chloride in pyridine at 0°.

A consideration of Fig. 1 shows that the so-called "tri-*O*-tosylsucrose" does in fact contain 1',6,6'-tri-*O*-tosylsucrose as the main component. However, the compound is only present to an extent of about 0.29 mole per mole of sucrose reacted. The fact that the compound was formed in an amount more than twice that of any other tri-*O*-tosylsucrose shows that the 1'-position is substantially more reactive than any secondary hydroxyl group. Consequently, as was discussed above, the uncharacterized di-*O*-tosylsucrose (fraction D) can be expected to consist mainly of 1',6- and 1',6'-di-*O*-tosylsucrose. In this respect, it is of interest to note that Hockett and Downing (2) found 2,3:4,6-di-*O*-isopropylidene-L-sorbose to undergo tosylation half as rapidly as 1,2:3,4-di-*O*-isopropylidene-D-galactose. The results clearly render it unlikely that sucrose can be acylated preferentially in high yield at the 6- and 6'-positions only. This conclusion is substantiated by the foregoing results of a ditosylation experiment. The tritylation of sucrose has been shown (17) to yield 1',6,6'-tri-*O*-tritylsucrose pentaacetate in 45% yield. Table II describes the composition of the product obtained on a tritosylation of sucrose at  $-18^{\circ}$ . It is seen that the course of the reaction was not appreciably affected by the lowering of the reaction temperature.

TABLE II  
Chromatography of "sucrose tritosylate"

	Penta- and tetra- <i>O</i> -tosylsucrose	Tri- <i>O</i> -tosylsucrose		Di- <i>O</i> -tosylsucrose	
		Fraction A	Fraction B	Fraction C*	Fraction D
Weight of material (g)	2.0	3.11	1.5	0.75	2.85
Per cent of mixture (w/w)	20.0	31.1	15.0	7.5	28.5
$R_f$ value†	0.9 and 0.65	0.40	0.40	0.15	0.15

NOTE: The material, 10 g, was prepared at  $-18^{\circ}$ .

\*Crystalline 6,6'-di-*O*-tosylsucrose.

†On paper impregnated with silicic acid using the solvent system diisobutyl ketone:acetic acid:water (40:25:5).

TABLE III  
Chromatography of "sucrose ditosylate"

	Tetra- <i>O</i> -tosylsucrose	Tri- <i>O</i> -tosylsucrose		Di- <i>O</i> -tosylsucrose	
		Fraction A	Fraction B	Fraction C*	Fraction D
Weight of material (g)	1.04	2.79	1.74	1.85	2.60
Per cent of mixture (w/w)	1.04	27.9	17.4	18.5	26.0
Sulphur content (%)					
Found:	12.96	11.82	11.76	10.12	10.11
Calc.:	13.38	11.93	11.93	9.85	9.85

NOTE: The material, 10 g, was prepared at  $0^{\circ}$ .

\*Crystalline 6,6'-di-*O*-tosylsucrose.

The product formed on the ditosylation of sucrose was analyzed chromatographically. The results are presented in Table III and Fig. 2. A comparison of the yields reported in Figs. 1 and 2 shows that the ditosylation produced, as would be expected, a greater yield of 6,6'-di-*O*-tosylsucrose (fraction C). The yield of other sucrose ditosylates (fraction D) was, however, about the same as that obtained in the tritosylation. This result clearly indicates that the 6- and 6'-positions both undergo tosylation somewhat more rapidly than does the 1'-position. The fact that the ditosylation produced nearly as much 1',6,6'-tri-*O*-tosylsucrose as did the tritosylation clearly reflects the greater reactivity of the three primary positions over the secondary positions of sucrose.

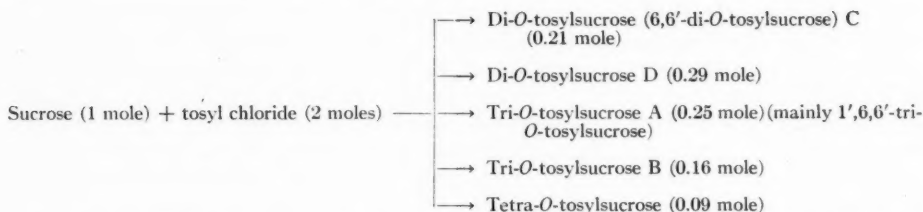


FIG. 2. Distribution of the tosylated sucroses formed in the reaction of 1 mole of sucrose with 2 moles of tosyl chloride in pyridine at 0°.

#### EXPERIMENTAL

The melting points are uncorrected and were determined on a microheating stage. Mallinckrodt reagent grade (100-mesh, lot 2847) silicic acid was used throughout.

##### "Tri-*O*-tosylsucrose"

A preparation was made at 0° in 95% yield using the method described by Hockett and Zief (9) and had a softening point of 65° to 85°,  $[\alpha]_D +43^\circ$  (*c*, 2.88 in chloroform). Anal. Calc. for  $C_{33}H_{40}O_{17}S_3$ : S, 11.93%. Found: S, 11.11%. The composition of this product is described in Table I and in Fig. 1.

A second preparation was made at -18° in a refrigerated bath using the following procedure. Sucrose, 34.2 g (0.1 mole), was dissolved in dry pyridine, 600 ml, by refluxing the mixture for a short time. The solution was then cooled to -18° with vigorous stirring for 2 hours. Tosyl chloride, 57 g (0.3 mole), was dissolved in 150 ml of dry pyridine and the solution was added dropwise to the solution of sucrose over a period of 2 hours. The reaction was left with continuous stirring at -18° for 5 days. The product, isolated in the usual manner, weighed 74.3 g (92.5%) with m.p. 65-85°,  $[\alpha]_D +42^\circ$  (*c*, 2.5 in chloroform). Anal. Calc. for  $C_{33}H_{40}O_{17}S_3$ : S, 11.93%. Found: S, 11.66%. The composition of this product is described in Table II.

##### Chromatography of "Tri-*O*-tosylsucrose" on Paper Impregnated with Silicic Acid

The silicic-acid-impregnated paper was prepared by the method of Marinetti, Erbland, and Kochen (16) but using Whatman No. 3 chromatographic paper. The chromatograms were developed by the descending method using the solvent system, diisobutyl ketone:acetic acid:water (40:25:5). The dried paper was immersed in 0.01% aqueous Rhodamine 6G solution (16) and examined under ultraviolet light in a dark room. Both "tri-*O*-tosylsucrose" preparations gave spots of similar intensities having  $R_f$  values of 0.15, 0.40, 0.65, and 0.90.

##### Silicic Acid-Column Chromatography of "Tri-*O*-tosylsucrose"

The silicic acid, 200 g, was packed as a slurry in chloroform in a 2.5-cm (diameter) column. The "tri-*O*-tosylsucrose", 9-10 g, was dissolved in 20 ml of chloroform and applied to the top of the column. The column was then developed with the solvent system, diisobutyl ketone:acetic acid:water (40:25:5). After the solvent front had displaced all of the chloroform from the column, 3-ml fractions were collected at a rate of 1 tube every 2 minutes. A total of 110 tubes were collected. Further eluant was free of material. The tubes were examined by spotting on paper and applying the Rhodamine 6G color test. Five different zones were apparent in the series of tubes. After the tubes within each zone had been combined, the solvent was removed *in vacuo* and the weights of the residues were determined.

The results are given in Tables I and II. Crystals were deposited in the fraction which proved to correspond to the fraction of di-*O*-tosylsucroses. In the case of the "tri-*O*-tosylsucrose" prepared at 0°, the crystalline substance (fraction C) was collected before evaporation of the solvent. The extremely fine needles, 0.92 g, m.p. 101–106°, were extremely soluble in methanol, but sparingly soluble in water, ethanol, or chloroform. After three recrystallizations from water, this compound melted at 108–110°,  $[\alpha]_D^{25} +54^\circ$  (*c*, 1.66 in ethanol). The compound only reduced Fehling's solution after acid hydrolysis. Anal. Calc. for  $C_{26}H_{34}O_{15}S_2$ : C, 47.8%; H, 5.22%; S, 9.85%. Found: C, 47.2%; H, 5.29%; S, 10.12%. The experiments described below established the compound to be 6,6'-di-*O*-tosylsucrose.

*6,6'-Diido-6,6'-dideoxysucrose Hexaacetate*

6,6'-Di-*O*-tosylsucrose (fraction C), 0.1 g, was dissolved in 1 ml of dry pyridine, and 2 ml of acetic anhydride and left at 4° for 2 days. The acetate, 126 mg, was isolated in the usual manner. The amorphous solid resisted crystallization. The substance, 76.5 mg, was dissolved in 15 ml of 10% sodium iodide in acetone and the solution was heated at 120° for 16 hours. The sodium tosylate, 36.2 mg, which precipitated represented a replacement of two tosyloxy groups. The syrupy product, 59.2 mg, was isolated in the usual manner. Its nuclear magnetic resonance spectrum was devoid of signals for the aromatic and *C*-methyl hydrogen atoms of the tosyl group. Anal. Calc. for  $C_{24}H_{32}O_{15}I_2$ : I, 31.4%. Found: I, 29.3%.

*Monoiodomonodeoxymono-O-tosylsucrose Hexaacetate*

The syrupy di-*O*-tosylsucrose (fraction D), 2.11 g, remaining after the removal of the crystalline 6,6'-*O*-tosylsucrose (see above) was acetylated and the product was subjected to the sodium iodide in acetone treatment. The amount of sodium tosylate recovered represented a replacement of 1.1 tosyloxy groups.

*Reaction of Tri-O-tosyl Sucroses A and B with Sodium Iodide*

Acetylated samples of tri-*O*-tosylsucrose fractions A, 135 mg, and B, 128 mg, were treated as described above with 10% sodium iodide in acetone. The amounts of sodium tosylate recovered were 49.69 mg and 41.58 mg, respectively. These amounts represent the replacement of 1.87 and 1.63 tosyloxy groups per mole, respectively. Anal. Calc. for  $C_{29}H_{36}O_{16}I_2S$ : I, 30.7%. Found: I, 28.6% (fraction A) and I, 27.8% (fraction B).

*1',2:3,6:3',6'-Trianhydrosucrose Diacetate*

Tri-*O*-tosylsucrose A, 200 mg, was dissolved in methanol *M* in sodium methoxide and the solution was refluxed for 30 minutes. The reaction mixture was evaporated to dryness and the residue was shaken with boiling pyridine, 50 ml, for 15 minutes. After the mixture was cooled to 0°, 10 ml of acetic anhydride was added. The syrupy product, isolated in the usual manner, crystallized on trituration with methanol. The yield was 71.6 mg (77.4% of theory) of 1',2:3,6:3',6'-trianhydrosucrose diacetate, m.p. 179–181°, undepressed when admixed with an authentic specimen.

*Periodate Oxidation of the Tri-O-tosylsucroses A and B*

To a sample of the tosyl ester, 0.05 millimole, dissolved in 80 ml of glacial acetic acid, 10 ml of 0.25 *N* sodium metaperiodate was added and the solution made up to 100 ml with water. Aliquots, 10 ml, were taken at suitable time intervals and were reacted with potassium iodide and an excess of 0.1 *N* sodium thiosulphate solution (18). The excess thiosulphate was determined by titration to the starch end point with standard

0.005 *N* iodine solution. Periodate was not consumed in the blank determinations. The periodate uptake by fraction A was 0.61, 1.53, 2.02, 2.18, 2.41, 2.78, and 2.82 moles of oxidant per mole of A after 0.5, 1, 10, 18, 32, 85, and 108 hours. The periodate uptake by fraction B was 0.49, 0.51, 0.98, 1.18, 1.59, 1.72, and 1.75 moles of oxidant per mole of B after 0.5, 1, 10, 18, 32, 85, and 108 hours.

#### *Ditosylation of Sucrose*

Sucrose, 34.2 g (0.1 mole), was dissolved in 600 ml of dry pyridine and cooled to 0°; tosyl chloride, 38 g (0.2 mole), was added and the reaction mixture was kept at 0° for 5 days. The reaction mixture was then shaken at room temperature with 5 ml water for 30 minutes. The excess pyridine was removed *in vacuo* at 40° to leave a thick syrup. This syrup was dissolved in 1 liter of chloroform and washed with 200 ml of ice-cold 2 *N* sulphuric acid followed by 200 ml of saturated sodium bicarbonate and finally with 200 ml of water. The chloroform solution, after drying over anhydrous sodium sulphate, was evaporated to a dry, amorphous solid, 56 g (86% of theory). Chromatography on silicic-acid-impregnated paper revealed three components, *R<sub>f</sub>* values, 0.13, 0.38, and 0.6. Column chromatography of 10 g of the material allowed the isolation of the fractions described in Table III and in Fig. 2.

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# THE STRUCTURE OF SANDARACOPIMARIC ACID<sup>1</sup>

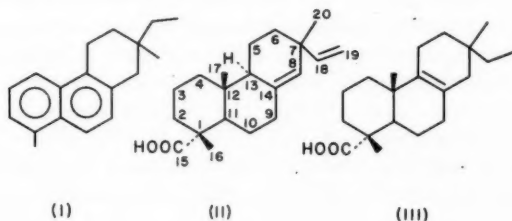
O. E. EDWARDS, A. NICOLSON,<sup>2</sup> AND M. N. RODGER<sup>2</sup>

## ABSTRACT

Sandaracopimaric acid has been shown to be 7-epipimara-8(14),18-dienoic acid (II), and Ukita's acid to be 7-epi-13 $\beta$ -pimara-9(14),18-dienoic acid (VI). A hydroxyl-containing acid from Sandarac resin is described.

Sandaracopimaric acid was isolated by Henry (1) and by Tschirch and Wolff (2) from the resin of the N. African sandarac tree (*Callitris quadrivalvis*). Recently an improved isolation procedure was described by Petru and Galik (3), who also demonstrated that the acid belonged to the pimaric group. They claimed (4) that both pimaric acid and sandaracopimaric acid gave the same partial dehydrogenation product I and hence had the same configuration at C-7. Even if this conclusion had been correct their work left the location of the double bond and the stereochemistry at the other asymmetric centers unknown.

In continuance of our interest in the stereochemistry of the pimaric acids<sup>3</sup> we have examined sandaracopimaric acid, and proved it to be the C-7 epimer (II) of pimaric acid (7-epipimara-8(14),18-dienoic acid).<sup>4</sup>



Using the method of Petru and Galik (3) we obtained an ether-soluble ammonium salt from the resin. This was converted into the sodium salt, which was then precipitated from its aqueous solution by addition of concentrated sodium hydroxide solution. The precipitate did not crystallize readily, so the acids liberated from it were chromatographed on silica gel. In this way a 2.2% yield of sandaracopimaric acid and a 1.3% yield of a higher melting acid were obtained. The latter had m.p. 270° and  $[\alpha]_D -11^\circ$  in ethanol. The melting point is close to that of sandaricinolic acid (2), but our analytic figures, which correspond to a hydroxypimaric acid, are widely different from those of Tschirch and Wolff. The infrared spectrum of the high melting acid had rather weak bands which could be ascribed to a vinyl group and a trisubstituted double bond, and a strong hydroxyl band at 3360  $\text{cm}^{-1}$ . We hence suggest that it is a hydroxypimaric acid.

<sup>1</sup>Manuscript received January 12, 1960.

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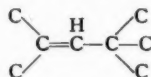
<sup>2</sup>National Research Council of Canada Postdoctorate Fellow.

<sup>3</sup>We wish to thank Dr. R. Howe, who first aroused our interest in sandaracopimaric acid.

<sup>4</sup>It seems desirable to have a systematic nomenclature for the pimaric acids, in particular to designate transformation products. However, the trivial names for the natural acids provide a convenient shorthand. We suggest that pimaric acid be designated pimara-8(14),18-dienoic acid, from which the other names follow as illustrated in the text. We do not consider the configuration at C-7 in pimaric acid to be settled, hence avoid commitment on this point.



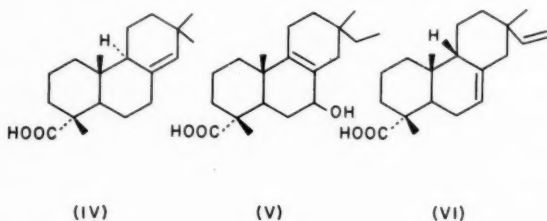
The physical constants for sandaracopimaric acid, m.p. 169°,  $[\alpha]_D -20^\circ$  in ethanol, were in good agreement with those reported by the Czech workers. Its rotatory dispersion curve was plain and negative. Its infrared spectrum suggested the presence of a vinyl group ( $\nu_{\max}$  913 and 994  $\text{cm}^{-1}$ ) but there was no clear band corresponding to a trisubstituted double bond. The acid was rapidly reduced in the presence of palladium to a dihydro derivative, m.p. 178° (Petru and Galik (3) report m.p. 180°), which now gave a spectrum containing a band at 824  $\text{cm}^{-1}$  ( $\text{>C=C<}^{\text{H}}$ ) but lacking the vinyl absorption. The N.M.R. spectrum of the dihydro compound contained a single signal in the vinyl hydrogen region which was not split by coupling with adjacent hydrogens (band width ca. 4 c.p.s.). This suggests the presence of the system



in the acid.

The presence of the pimaric acid skeleton and the isopimaric configuration at C-7 were next demonstrated by conversion of dihydrosandaracopimaric acid to 7-epipimar-13-enoic ( $\Delta^{13}$ -dihydroisopimaric) acid (III) using dry hydrogen chloride in chloroform (5). Since a nuclear double-bond location at 8(14) is the only one consistent with the N.M.R. spectrum and formation of III, and since C-13 is the only remaining center at which sandaracopimaric acid can differ from isopimaric acid, it must have structure II.

This conclusion was confirmed in the following way. Sandaracopimaric acid was hydroxylated with osmium tetroxide. The main product was a diol acid, m.p. 255°, in which the vinyl group had been oxidized. The glycol system was rapidly cleaved by periodic acid to an aldehyde acid, m.p. 215°. On Wolff-Kishner reduction this gave 19-norpimar-8(14)enoic acid (IV), identical in all respects with the gem-dimethyl acid prepared earlier from pimaric acid (6). This observation proves the identity of double-bond location and C-13 configuration in pimaric and sandaracopimaric acids, and hence structure II must correctly represent the latter.<sup>5</sup>



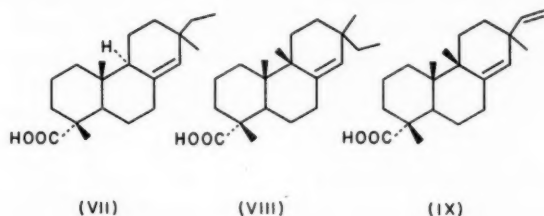
This finding removes the last doubt about the structure and stereochemistry of Ukita's acid (5). There was slight possibility that this acid had structure II although no obvious mechanism existed for the transformation of its dihydro derivative to V with selenium dioxide under mild conditions. The rotatory dispersion curve did not exclude II from consideration (7). However, the above results coupled with the rotatory dispersion now require that the acid be 7-epi-13β-pimara-9(14),18-dienoic acid (VI).

Wenkert has pointed out<sup>6</sup> that the rotatory dispersion curves of dihydropimaric (VII)

*The rotatory dispersion observations of Bose and Struck (7) provide an important addition to the body of evidence (6, 8, 9) suggesting that the C-13 hydrogen in pimaric acid is  $\alpha$  oriented.*

<sup>5</sup>Personal communication from Professor E. Wenkert.

and dihydroisopimaric (VIII) acids (7) are readily interpreted if a small positive contribution from the asymmetric centers in ring A is superimposed on the positive and negative plain curves due to the two mirror image situations in ring C. Extending this



argument, since sandaracopimaric acid has a plain negative curve the unknown pimaric acid IX whose ring C is the mirror image of that in II should have a plain positive curve. Hence cryptopimaric acid which has a plain negative curve (7) cannot be this isomer and hence must be a double-bond isomer. Bruun, Ryhage, and Stenhagen (9) concluded that cryptopimaric acid had structure II on the basis of mass spectrometry. This cannot be correct unless the physical constants of cryptopimaric acid are in error. However, their results do suggest the great importance of the C-13 stereochemistry in determining the fragmentation pattern when the nuclear double bond is in the 8(14) position. The uncertainty as to whether this applies to other double bond isomers, and the probable large effect of the vinyl group on the rotatory dispersion curve<sup>7</sup> make it unwise to suggest a structure for cryptopimaric acid at present.

#### EXPERIMENTAL

Unless otherwise stated, rotations were of ethanol solutions, infrared spectra were of Nujol mulls, and melting points were taken on a Kofler hot stage.

##### *Sandarac Resin Acids*

Commercial sandarac resin (900 g) dissolved nearly completely in ether. Ammonia was bubbled through the ether solution until precipitation ceased. The insoluble ammonium salts were removed by filtration and the filtrate extracted with 2% sodium hydroxide solution. The aqueous solution of sodium salts was acidified using 2% acetic acid, the acids collected on a filter, and washed well with water (yield 169 g). The sodium salts of this acid mixture did not crystallize readily, hence the acids were chromatographed on silica gel.

A benzene solution of approximately half the acid (87 g) was added to a column of 100- to 200-mesh silica gel (1.3 kg) and 100 cc eluate fractions collected.

Eluant	Fraction	Weight, g	Remarks
Benzene	1-9	4.5	Amorphous
Benzene-ether 20:1	10-14	6.4	Amorphous
Benzene-ether 10:1	15-20	26.2	8.8 g crystalline material
Benzene-ether 3:1	20-30	9.6	Amorphous
Benzene-ether 1:1	31-44	18.6	5.4 g crystalline material

The remaining fractions did not crystallize.

<sup>7</sup>Hydrogenation of the vinyl group of sandaracopimaric acid reverses the sign of rotation, hence presumably the sign of the rotatory dispersion curve.

*Sandaracopimaric Acid*

The yield of crude crystals from fractions 15–20 was 8.8 g (2.2% of the resin). The acid was purified by recrystallization from aqueous methanol, recrystallization of its sodium salt, and further recrystallization of the acid. It then had m.p. 169°,  $[\alpha]_D -20^\circ$  (c, 2.6). Its infrared spectrum had bands at 913 and 994  $\text{cm}^{-1}$  (vinyl group), 825  $\text{cm}^{-1}$  (very weak) ( $\text{>C=C<}^{\text{H}}$ ), and at 1692  $\text{cm}^{-1}$  ( $-\text{COOH}$ ). Its rotatory dispersion curve was plain and negative, with  $[\alpha]_{460} -50^\circ$  and  $[\alpha]_{290} -250^\circ$ .

*The Hydroxy Acid*

The yield of crude crystals from fractions 31–44 was 5.4 g (1.3% of the resin). When recrystallized from aqueous methanol it separated as plates, m.p. 270°,  $[\alpha]_D -11^\circ$  (c, 0.8). Found: C, 75.59; H, 9.74. Calc. for  $\text{C}_{20}\text{H}_{30}\text{O}_3$ : C, 75.43; H, 9.50. Its infrared spectrum had rather weak bands at 904 and 987  $\text{cm}^{-1}$  (vinyl group) and 822  $\text{cm}^{-1}$  ( $\text{>C=C<}^{\text{H}}$ ), a strong band at 3360  $\text{cm}^{-1}$  (hydroxyl group), and a band at 1695  $\text{cm}^{-1}$  ( $-\text{COOH}$ ).

*Dihydrosandaracopimaric Acid*

Sandaracopimaric acid (200 mg) in 15 ml of ethanol was reduced with hydrogen in the presence of 150 mg of presaturated 30% palladium on charcoal. In 5 minutes 16.3 ml of hydrogen was absorbed (calc. for 1 mole, 16.1 ml). The product was recrystallized three times from aqueous methanol giving 128 mg of needles, m.p. 174–178°,  $[\alpha]_D +21^\circ$  (c, 1.83). Found: C, 78.78; H, 10.54. Calc. for  $\text{C}_{20}\text{H}_{32}\text{O}_2$ : C, 78.94; H, 10.52. Infrared spectrum:  $\nu_{\text{max}}$  1692  $\text{cm}^{-1}$  ( $-\text{COOH}$ ); 824  $\text{cm}^{-1}$  ( $\text{>C=C<}^{\text{H}}$ ).

*Isomerization of Dihydrosandaracopimaric Acid*

Dry hydrogen chloride was passed into a solution of 73 mg of dihydrosandaracopimaric acid in dry ethanol-free chloroform at  $-5^\circ$  for 4 hours. The solution was then washed free of mineral acid with water, dried, and evaporated. The product (58 mg) crystallized from aqueous acetone as needles, m.p. 109–112°,  $[\alpha]_D +75^\circ$  (c, 1.0 in chloroform). It did not depress the melting point of  $\Delta^{13}$ -dihydroisopimaric acid (5) (m.p. 109–112°) and X-ray powder patterns of the two substances were identical.

*Hydroxylation of Sandaracopimaric Acid*

A solution of 636 mg of sandaracopimaric acid and 530 mg of osmium tetroxide in 10 ml of dry ether was left overnight at  $0^\circ$ . The black precipitate (1.2 g) was collected by filtration. It was then heated for 1 hour on a steam bath in 15 ml of water containing 2.7 g of mannitol and 0.5 g of sodium hydroxide. The resulting solution was acidified with acetic acid and the precipitated acid collected by filtration. This was boiled with methylene chloride to remove more soluble material, and the residue recrystallized three times from methanol. The diol acid separated as needles (410 mg), m.p. 255°,  $[\alpha]_D +39^\circ$  (c, 0.35). Found: C, 71.58; H, 9.75. Calc. for  $\text{C}_{20}\text{H}_{32}\text{O}_4$ : C, 71.39; H, 9.59. Infrared spectrum:  $\nu_{\text{max}}$  825  $\text{cm}^{-1}$  ( $\text{>C=C<}^{\text{H}}$ ), 1685  $\text{cm}^{-1}$  ( $-\text{COOH}$ ).

*Aldehyde Acid*

A solution of 200 mg of the above diol acid in 80 ml of aqueous dioxane (10% water) containing 290 mg of periodic acid was left for 1 hour at room temperature in the dark. The reaction mixture was then concentrated to around 6 ml under reduced pressure,

water added, and the solution extracted with methylene chloride. The methylene chloride solution was washed with water, dried, and evaporated, leaving 170 mg of crystalline residue. This was absorbed from benzene on 4 g of silica gel. Benzene eluted a small quantity of material. Benzene-ether (50:1, 40 ml fractions) eluted the bulk of the compound. Fractions 2 and 3 had m.p. 200–215° (evacuated capillary). These were combined and recrystallized twice from ether-hexane giving 141 mg, m.p. 215° (evacuated capillary),  $[\alpha]_D -2^\circ$  (*c*, 1.3). Found: C, 74.89; H, 9.31. Calc. for  $C_{19}H_{28}O_3$ : C, 74.96; H, 9.27. Infrared spectrum:  $\nu_{max}$  2700, 1727  $cm^{-1}$  (—CHO), 1693  $cm^{-1}$  (—COOH), 823  $cm^{-1}$  ( $\text{>C=C<}^H$ ).

#### 19-Norpimar-8(14)-enoic Acid

A solution of the above aldehyde acid (54 mg) in 2 ml of triethylene glycol and 0.5 ml of 95% hydrazine was heated on a steam bath for 30 minutes and at 140° for 30 minutes under an air condenser. Potassium hydroxide (0.64 g) was then added cautiously, the temperature raised to 205°, and maintained at that temperature for 4 hours, while a slow stream of nitrogen was introduced halfway down the condenser. The reaction mixture was then cooled, diluted with water, and extracted with methylene chloride. The methylene chloride was extracted with dilute sodium hydroxide solution, then the combined aqueous layers carefully acidified with 6 *N* sulphuric acid. The acid was again extracted into methylene chloride, the solution washed with water, dried, and distilled. The residual solid was recrystallized from methanol, giving 44 mg of needles, m.p. 238°,  $[\alpha]_D +18^\circ$  (*c*, 0.6). This did not depress the melting point of the gem-dimethyl acid from pimaric acid (6), m.p. 238°. Their X-ray powder patterns and infrared spectra were identical.

#### ACKNOWLEDGMENTS

We wish to thank Professor A. K. Bose for sending his manuscript before publication and for the rotatory dispersion curve of sandaracopimaric acid, Professor E. Wenkert for valuable comments on the rotatory dispersion curves, Professor F. A. L. Anet for the N.M.R. spectrum, Dr. M. Przybylska and Miss C. Philo for the X-ray pattern comparisons, Mr. R. Lauzon for the infrared spectra, and Mr. A. Knoll for technical assistance.

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# MOLECULAR AREAS OF SOAPS AT THE SURFACE OF LATEX PARTICLES<sup>1</sup>

R. J. ORR AND L. BREITMAN

## ABSTRACT

The molecular area (i.e., the area occupied by a molecule of soap adsorbed on a surface) has been determined for a number of anionic, cationic, and non-ionic emulsifiers, adsorbed on latex particles. Measurements were made by surface tension and electron microscopic techniques. The composition of the polymer did not affect the molecular area of either anionic or cationic soaps. When a mixture of non-ionic and anionic soaps was used, interaction between the soaps prevented application of the conventional methods for measuring molecular area. The interaction is manifested by a decrease in the area occupied by an anionic soap molecule which can be explained in terms of reduction in electrostatic repulsive forces between ionic soap molecules. The configuration of the polyethylene oxide chain of the non-ionic on the surface of the latex particle is deduced to be that of caterpillarlike folds.

## INTRODUCTION

The emulsion of rubber in water, known to the rubber industry as latex, offers special opportunities for study of physical properties of soaps at the polymer-water interface. This fact was first noted and used by Maron (1), who determined the minimum area which soap molecules in a monolayer occupy at the polymer-water interface. The specific property of the latex on which such studies depend is the ability of the polymer-water interface to adsorb more soap after the synthesis of the latex is complete. The main objectives of the study reported here were

- (i) to increase the applicability of titration methods in determining latex particle size and surface areas of adsorbed soaps,
- (ii) to learn something about the molecular geometry of the emulsifier at the interface which might be helpful in developing hypotheses concerning the mechanism of stabilization of latex.

## THEORETICAL

### *Soap Titration in One-Component Systems*

The area ( $A$ ) occupied by an adsorbed soap molecule may be obtained from Maron's equation

$$[1] \quad A = \frac{A_T}{N(S_1 + S_a)}$$

where  $A_T$  = surface area/g polymer,

$S_1$  = number of moles of soap adsorbed/g polymer in final latex,

$S_a$  = additional number of moles of soap adsorbed/g polymer, when sufficient soap is added to obtain the critical micelle concentration (c.m.c.) in the aqueous phase,

$N$  = Avogadro's number.

Suppose that two different substrates are dispersed in water, that  $A_T$  is the same for both dispersions, and that soap is added to the aqueous phase until the c.m.c. is reached. The substrate with the greater affinity for the soap will adsorb more soap and, from equation [1], it follows that the value of  $A$  will be lower for this substrate. Comparison of affinities of soap for polymer by this method is not valid when the c.m.c. is so high

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Contribution from Polymer Corporation Limited, Research and Development Division, Sarnia, Ontario.

that both substrates adsorb sufficient soap to form a condensed and incompressible monolayer. Since these conditions do not, in general, exist, low values of  $A$  may be taken as evidence of high affinity of substrate for soap.

#### *Soap Titration in Two-Component Systems*

If two portions of the same latex are titrated to the c.m.c., one with soap A and the other with soap B, then, according to Maron, the following relation holds:

$$[2] \quad S_A^A A^A = S_B^B A^B = A_T - S_I A N.$$

The superscripts refer to the two soaps, A and B.

Equation [2] enables one to determine areas of soaps which, for practical reasons, cannot be used to prepare the original latex. This equation is valid if the following conditions hold:

(i) no desorption of the original soap occurs during titration with a different soap, and

(ii) at the titration end point, the area per molecule of the initial soap corresponds to its area at its own c.m.c.

As is shown later, these conditions are not always fulfilled.

#### *Determination of $A_T$ by Electron Microscopy*

When the latex is not monodisperse, results of electron microscope analysis are readily expressed by the number average particle diameter ( $\bar{X}$ ) and a standard deviation ( $\sigma$ ). It may then be shown (see Appendix) that  $A_T$  is given by

$$[3] \quad A_T = \frac{6}{\bar{X}d} \left( \frac{\bar{X}^2 + \sigma^2}{\bar{X}^2 + 3\sigma^2} \right)$$

where  $d$  is the polymer density.

#### *Use of Surface Tension to Determine Critical Micelle Concentration*

The surface tension method was selected for the determination of the c.m.c. of both ionic and non-ionic soaps, since the electrical conductivity method obviously cannot be used for non-ionics. Although the validity of the surface tension method for ionic soaps has been questioned (2), we have found the procedure to be satisfactory (see Results). The theoretical basis for this procedure with non-ionics has been provided by Bury (3). Some insight as to the significance of a surface tension measurement with an ionic soap may be provided by the following argument.

Only one of the ions of a soap is normally capillary-active, but the adsorption of capillary-active ions on the surface sets up an electrical field which tends to attract ions of the capillary-inactive species.

The Gibbs adsorption isotherm for a uni-univalent emulsifier may then be written as

$$-d\gamma/RT = \Gamma_+ d \ln a_+ + \Gamma_- d \ln a_-$$

where  $a$  and  $\Gamma$  represent bulk activities and surface excesses respectively of the two ions. At low concentrations of emulsifier, the activities of the ions are equal (4).

The substitution

$$a^+ = a^- \equiv a$$

gives

$$-d\gamma/RT = d \ln a (\Gamma_+ + \Gamma_-).$$



At high ionic strength, where  $\Gamma_+ \rightarrow \Gamma_-$ , the above equation reduces to the expression given by Pethica (5) for these conditions.

A plot of  $\gamma$  versus  $\ln c$  (or  $\ln a$ ) is usually a curve with a more or less sharp change in slope at a concentration which is assumed to be the critical micelle concentration.

#### CHEMICALS

The various commercial soaps used in this investigation are listed below with trade names, formulae, and suppliers.

Trade name	Formula	Supplier
Agent 180 BK	$(C_9H_{19})_3 \text{C}_6\text{H}_4 \text{O} (C_2H_4O)_{15}H$	Chemical Developments of Canada
Armac 10	$C_{10}H_{21}NH_2 : CH_3COOH$	Armour Company
Armac 14	$C_{14}H_{31}NH_2 : CH_3COOH$	Armour Company
Brij 30	$C_{12}H_{25}O(C_2H_4O)_4H$	Atlas Powder Co.
Daxad 11	Polymerized sodium salt of alkyl naphthalene sulphonic acid	Dewey and Almy
Dresinate 214	$C_{20}H_{43}O_2K$	Hercules Powder Co.
Igepal CO-880	$C_9H_{19} \text{C}_6\text{H}_4 \text{O} (C_2H_4O)_{12}H$	General Aniline Corp.
LOP-100	$C_9H_{19} \text{C}_6\text{H}_4 \text{O} (C_2H_4O)_{20}H$	Chemical Developments of Canada
Nacconol	$C_{12}H_{25} \text{C}_6\text{H}_4 \text{SO}_3Na$	National Aniline Corp.
Rosin amine D	$C_{19}H_{37}NH_2 : CH_3COOH$	Hercules Powder Co.

#### EXPERIMENTAL

Impurities in soap may be surface-active or inert. Electrolytes, apart from a slight effect on the critical micelle concentration of the soap, are of no importance. Surface active contamination is serious since small amounts of such impurities have a strong influence on the  $\gamma - \ln c$  relation. Miles and Shedlovsky (6) found that minima in the surface tension - concentration relation indicate surface-active impurities. Hutchinson (7) showed that small amounts of octyl alcohol had a pronounced effect on the surface excess of sodium dodecyl sulphate.

The  $C_{10}$  and  $C_{14}$  *n*-alkyl amines and the rosin amine were purified by steam distillation of the amine regenerated from the commercial emulsifier. The amine was reacidified with C.P. glacial acetic acid. Nacconol, Dresinate 214, and cetyl pyridinium chloride were used without further purification. Other ionic emulsifiers were prepared from C.P. reagents. No sharp minima in the surface tension - concentration relation, characteristic of surface active contamination, were observed with these emulsifiers. A much smaller minimum was observed with Armac 14, the acetate of a  $C_{14}$  *n*-alkyl amine, but, since this disappeared when electrolyte was added, it is suggested that this minimum is associated not with impurities, but perhaps with absorption of micelles on the surface, as reported by Judson (8), and Ruysen and Maebe (9). The Nacconol was 93% pure, having 6% sodium sulphate and 1% volatile (10). The Dresinate 214 and cetyl pyridinium chloride were 100% active. The non-ionic emulsifiers exhibited a distribution of ethylene oxide

content but were certified as 100% active by the suppliers. Of the non-ionics, only Igepal CO-880 displayed a surface tension minimum ( $\sim 2$  dynes/cm).

All surface tension measurements were done with a CENCO du Nuoy ring tensiometer. Readings were corrected for ring diameter and wire thickness by the method of Harkins (11).

Area/gram ratios were calculated from equation [3] with a polymer density of 0.94 for butadiene/styrene and 0.96 for butadiene/acrylonitrile and butadiene/methyl methacrylate copolymers (12).

#### Preparation of Latices

Latices stabilized with all three types of soap—anionic, non-ionic, and cationic—were prepared by conventional emulsion polymerization techniques. The reaction temperature was 50° C and the source of initiating free radicals was obtained by reaction of a ferrous iron – potassium pyrophosphate complex with diisopropyl benzene hydroperoxide. After 60 to 80% conversion of monomers to polymers, the reaction was stopped and residual monomers were removed by steam distillation. Coagulum formation during polymerization was objectionable since this made estimation of  $S_1$  difficult. It was possible to avoid excessive coagulum formation in all cases, except when cetyl pyridinium chloride was used. Determinations of the area of cetyl pyridinium chloride were made with two coagulum levels in the latex.

Comonomers used with butadiene were styrene, acrylonitrile, and methyl methacrylate. Monomer charge ratios were 70/30 butadiene/styrene and 66/33 butadiene/acrylonitrile, except where otherwise specified.

Electron microscope data on the above latices were determined and are shown in Table I.

TABLE I  
Electron microscope data on latices

Emulsifier	Soap in reaction per 100 parts monomer (parts)	Comonomer	Bd in comonomer charge (%)	Average particle diameter (Å)	Standard deviation ( $\sigma$ )
Dodecyl amine acetate	5.0	Styrene	70	915	60
		Styrene	70	1077	104
		Acrylonitrile	80	794	95
		Methyl methacrylate	80	950	146
Cetyl pyridinium chloride	3.0	Styrene	70	1340	10
	4.0			1237	90
	3.0			1028	57
Igepal CO-880, Nacconol	0.5*	Styrene	70	1129	236
	1.0*			1051	208
	1.5*			877	255
Igepal CO-880, K-oleate	0.5*	Styrene	70	1090	247
	1.0*			1026	183
	1.5*			870	187
Dresinate 214, Na fatty acid	—	Styrene	72	570	10
Dresinate 212, Dresinate 214	—	Styrene	50	600	10
Daxad 11, Nacconol	—	Acrylonitrile	67	600	10

\*Refers to anionic soap; non-ionic held constant at 5.0 parts.

### Soap Titration

The amount of soap necessary to reach the c.m.c in latex was determined from a plot of log (cc added soap) versus surface tension, as shown in Fig. 1. The soap was added

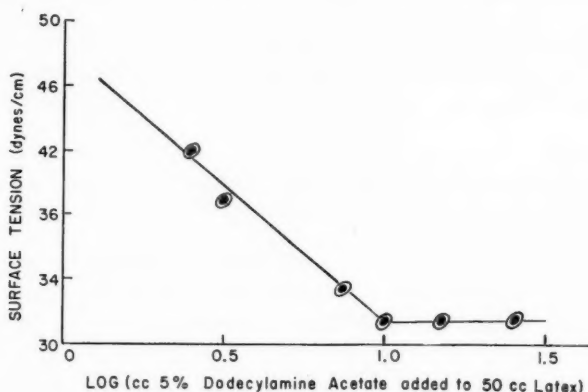


FIG. 1. Variation in surface tension with soap content for 80/20 butadiene-acrylonitrile latex.

to latex which had been adjusted to a solids content of 15%. The pH was maintained at fixed values to prevent hydrolysis of the soap. With cationic lattices, the pH was 4 and with anionic lattices, the pH was 10. Some experiments (where there was a high ratio of non-ionic to anionic) were done at two values of pH, 7 and 10. The temperature was maintained at  $26^{\circ} \pm 1^{\circ} \text{C}$ .

### RESULTS

Surface tension was plotted against logarithm of the concentration for anionic, cationic, and non-ionic soaps. The concentration at which there is a sharp change in the slope of the relation was taken at the c.m.c. Measured values of the c.m.c. were compared, when possible, with those calculated from an empirical equation due to Kleven (13):

$$[4] \quad \log \text{ c.m.c. (mole/liter) } = 2.26 - 0.231 (\text{length of surface active ion in } \text{\AA}).$$

TABLE II  
Critical micelle concentrations of ionic soaps by the surface tension method (pH = 7)

Soap	Critical micelle concentration (moles/liter)		
	Observed		Calculated from equation [4]
	% salt	0.1% NaCl	
Armac 10	$2 \times 10^{-3}$	$3 \times 10^{-3}$	$5 \times 10^{-3}$
Dodecyl amine acetate	$1 \times 10^{-3}$	$4 \times 10^{-3}$	$1 \times 10^{-3}$
Armac 14	$2 \times 10^{-3}$	$2 \times 10^{-3}$	$3 \times 10^{-3}$
Rosin amine acetate	$9 \times 10^{-3}$	$9 \times 10^{-3}$	
Cetyl pyridinium chloride	$6 \times 10^{-3}$	$8 \times 10^{-3}$	
Nacconol	$1.0 \times 10^{-3}$ *	$7 \times 10^{-4}$	
Potassium oleate	$9 \times 10^{-4}$	$1.8 \times 10^{-4}$	$1 \times 10^{-3}$

\* $2.1 \times 10^{-3}$  moles per liter  $\text{Na}_2\text{SO}_4$ .

TABLE III  
Critical micelle concentration of non-ionic soaps (pH = 7)

Soap	Hydrophobic group	C <sub>2</sub> H <sub>4</sub> O, units/molecule soap	Molecular weight	Critical micelle concentration	
				0% salt	0.1% NaCl
Triton X-45	Iso-octyl phenol	5	426	$0.6 \times 10^{-4}$	$0.64 \times 10^{-4}$
Brij 30	Lauryl alcohol	4	360	$1.25 \times 10^{-5}$	$4.3 \times 10^{-6}$
LOP-100	Nonyl phenol	20	1100	$1.8 \times 10^{-4}$	—
Brij 35	Lauryl alcohol	23	1200	$6.2 \times 10^{-5}$	$5.0 \times 10^{-5}$
Igepal CO-880	Nonyl phenol	32	1628	$1.5 \times 10^{-4}$	—

Results are listed in Tables II and III. Data in Table III may be compared with results obtained by a similar method by Hsiao, Dunning, and Lorenz (14). The value for LOP-100 agreed closely. The value for Igepal CO-880 was lower, possibly due to the masking effect of the minimum we observed in the surface tension-concentration plot. The good agreement between the calculated and observed values of the c.m.c. confirms the reliability of the surface-tension method.

#### Area of Cationic Soaps

In calculation of area/soap molecule ( $A$ ), the values of  $S_a$  in equation [1] were determined by subtracting the c.m.c. in water from the amount of soap necessary to reach the c.m.c. (or titration end point) in latex. The change in the c.m.c. in water caused by 0.1% NaCl (see Table II) has negligible effect on the calculated soap area. The areas of dodecyl amine acetate and cetyl pyridinium chloride at titration end point are shown in Table IV. The difficulty in obtaining good reproducibility with cetyl pyridinium chloride

TABLE IV  
Molecular areas of cationic soaps at titration end point (equation [1])

Soap	Comonomer	Bd in comonomer charge (%)	Molecular area (Å <sup>2</sup> )	Average
Dodecyl amine acetate	Styrene	70	22.6	25.6
	Styrene	70	25.0	
	Acrylonitrile	80	27.0	
	Methyl methacrylate	80	26.2	
Cetyl pyridinium chloride	Styrene	70	42.4	46.0
			41.5	
			54.0	

was due, as already mentioned, to the formation of coagulum during polymerization. The areas of dodecyl amine acetate indicate that there is little, if any, difference in the degree of binding of this soap to the different substrates.

Equation [2] was used to determine the areas  $A^B$  of cationic soaps which were not used in the polymerization of the latex. Values for  $A^A$  were the directly determined ones in Table III. Dodecyl amine acetate or cetyl pyridinium chloride was used as the emulsifier in the polymerization step. The molecular areas so determined are listed in Tables V and VI. The data in these tables indicate that the nature of the polymeric

TABLE V  
Molecular areas of cationic soaps at titration end point by comparative soap adsorption (equation [2])

Soap	Comonomer	Bd in comonomer charge (%)	Area covered by dodecyl amine acetate in original latex (%) <sup>*</sup>	$A^B$ molecular area ( $\text{\AA}^2$ )
Armac 10	Styrene	70	45	19.4
	Acrylonitrile	80	55	19.2
	Methyl methacrylate	80	64	17.2
Armac 14	Styrene	70	45	27.6
	Acrylonitrile	80	55	30.5
Rosin amine D	Styrene	70	45	26.5

<sup>\*</sup>% area covered" is defined by  $NS_1A/AT \times 100$ .

TABLE VI  
Molecular areas of cationic soaps at titration end point by comparative soap adsorption (equation [2])

Soap	Comonomer	Bd in comonomer charge (%)	Area covered by cetyl pyridinium chloride in original latex (%)	$A^B$ molecular area ( $\text{\AA}^2$ )
Armac 10	Styrene	70	70	20
Armac 14	Styrene	70	70	23

substrate does not significantly affect the molecular area of the cationic soaps at the interface.

The molecular areas of ARMAC 10 and ARMAC 14 may be compared with the value of  $26 \text{ \AA}^2$  for lauryl amine hydrochloride at the water-air interface reported by Harkins and co-workers (17).

#### Areas of Anionic Soaps

Two portions of an anionic latex were titrated, one with potassium oleate (B) and the other with the soap (A) whose area  $A^A$  is sought.  $A^A$  is calculated from equation [2] in which  $A^B$ , the area of the oleate molecule, was taken as  $28.2 \text{ \AA}^2$  (1). The results so obtained are shown in Table VII.

TABLE VII  
Molecular areas of anionic soaps at titration end point by comparative soap adsorption (equation [2])

Soap	Comonomer	Bd in comonomer charge (%)	Molecular area ( $\text{\AA}^2$ )
Sodium dodecyl benzene sulphonate	Styrene	72	32
			40
Dresinate 214	Acrylonitrile	66	34
			40
	Styrene	50	38
Daxad 11*	Acrylonitrile	66	38
			$12.8 \times 10^{22} \text{ \AA}^2/\text{g}$ soap

\*Determined by electron microscopy and titration with oleate.

It should be noted that there is some question about the accuracy of the area of the oleate molecule assumed here, since values as high as  $47 \text{ \AA}^2$  (15) have been reported. For two butadiene/styrene latices the total surface area, as measured by electron microscopy, compared well with that calculated from the values determined from the soap titration data. These results appear to substantiate the low value for the area of oleate.

The area of Daxad 11 ( $12.8 \times 10^{22} \text{ \AA}^2/\text{g}$ ) on a butadiene/acrylonitrile latex containing Nacconol compares reasonably well with the value of  $11.2 \times 10^{22} \text{ \AA}^2/\text{g}$  given by Maron (16) on a butadiene/styrene substrate.

#### *Molecular Areas of Non-ionic Soaps*

It was not possible to prepare latices with non-ionic soap alone in which the soap concentration in the aqueous phase was less than c.m.c. It was, therefore, impossible to obtain a titration end point on addition of soap and, accordingly, only a minimum value of the area per molecule could be directly determined. For a nonyl phenyl ethylene oxide condensate (Igepal CO-880) containing 30 moles ethylene oxide per mole nonyl phenol, a minimum value of  $120 \text{ \AA}^2/\text{molecule}$  was obtained by the procedure described for anionic and cationic soaps with the use of equation [1]. Separate portions of an undercovered anionic latex (i.e. a latex capable of adsorbing more soap at the oil-water interface) were titrated with potassium oleate and the non-ionic soap. Application of equation [2] to the titration data gave the values of molecular area listed in Table VIII.

TABLE VIII  
Molecular areas of non-ionic soaps at titration end point by comparative soap adsorption (equation [2])

Comonomer	Bd in comonomer charge (%)	Emulsifier	$\text{C}_{12}\text{H}_{25}\text{O}$ , units/molecule soap	Molecular area ( $\text{\AA}^2$ )
Styrene	72	Polyoxyethylene	30 (Igepal CO-880)	162
		Nonyl phenol	20	125
		Polyoxyethylene		
Styrene	50	Lauryl alcohol	4	40
		Polyoxyethylene		
		Nonyl phenol	20	110
Acrylonitrile	66	Polyoxyethylene		
		Nonyl phenol	30 (Igepal CO-880)	143
		Polyoxyethylene		
		Isopropyl phenol	5	28.1
		Polyoxyethylene		
		Dinonyl phenol	16	73

The correctness of these values, as well as of those in Tables V, VI, and VII, depends upon the validity of the two previously stated assumptions.

Another set of experiments was designed with the object of obtaining undercovered latex particles in which the fraction of surface occupied by the non-ionic could be varied over a wide range. This was accomplished by using varying ratios of non-ionic to ionic soap in the polymerization recipe. It was expected that interactions between the two types of soap in the adsorbed phase would be reflected in the observation that the molecular area at the titration end point is different when a second soap is present.

Separate portions of a given latex with a high ratio of non-ionic to ionic soap were titrated with an anionic soap (A) and a non-ionic soap (B) to obtain values of  $S_a^A$  and  $S_a^B$ . When the value of  $A^A$  was taken to be its characteristic value in the absence of a non-ionic, and the value of  $A^B$  was calculated from equation [2], these values of  $A^A$



and  $A^B$  led to a total area of the latex particles which exceeded by about 50% the total area directly determined by electron microscopy. This result demonstrated that equation [2] is inapplicable to systems containing mixtures of ionic and non-ionic soaps, either because of interaction of the two types of soap in the adsorbed phase, or because of displacement of one soap by the other. It was not possible, on the basis of our experiments, to decide between the two alternatives. However, if it is assumed that displacement does not occur, it is then possible to obtain estimates of the changes in molecular areas that resulted from the interaction of the two soap species.

Separate portions of a given latex containing known amounts of anionic soap ( $S_1^A$ ) and non-ionic soap ( $S_1^B$ ) may be titrated with an anionic soap (A) and a non-ionic soap (B) to obtain values of  $S_a^A$  and  $S_a^B$  respectively. The relation between  $A_T$  and the concentrations of adsorbed soap is

$$[5] \quad A_T/N = (S_1^A + S_a^A)A_z^{A*} + S_1^B A_z^{B*} = (S_1^B + S_a^B)A_y^{B*} + S_1^A A_y^{A*}.$$

$A_z^{A*}$  and  $A_z^{B*}$  are the molecular areas of anionic and non-ionic soap, respectively, at the titration end point with anionic soap.

$A_y^{A*}$  and  $A_y^{B*}$  are molecular areas of anionic and non-ionic soap, respectively, at the titration end point with non-ionic soap.

If it be assumed that the molecular area of a soap in an anionic/non-ionic soap mixture is independent of the relative concentrations of these soaps over the range investigated, one can write

$$[6] \quad A_z^{A*} = A_y^{A*} \equiv A^{A*}$$

and

$$[7] \quad A_z^{B*} = A_y^{B*} \equiv A^{B*}.$$

Values of  $A^{A*}$  and  $A^{B*}$  obtained from solution of equations [5], [6], and [7] are shown in Table IX. The asterisk symbol is used to differentiate molecular area in the mixed soap monolayer from that in a one-component monolayer.

TABLE IX  
Molecular areas of anionic soaps and Igepal CO-880 at titration end point  
(equations [5], [6], and [7])

Anionic emulsifier in polymerization		Area covered by:		Molecular area ( $\text{\AA}^2$ )	
Type	Parts	Original anionic	Igepal CO-880	Anionic	Igepal CO-880
Nacconol	0.5	4.1	59.0	18.1	126
Nacconol	1.0	6.5	54.0	19.0	131
Potassium oleate	0.5	4.6	70.0	19.5	130
Potassium oleate	1.0	8.4	60.0	21.0	123

The estimate for the molecular area of Igepal CO-880 in the mixed soap system (Table IX) is about  $30 \text{ \AA}^2$  less than the value based on methods that assume no soap interaction. This method of determining areas of the non-ionic soap in the presence of anionic soap was limited to Igepal CO-880 since other non-ionic soaps do not support polymerization. If the area in mixed soap systems is independent of the nature of the non-ionic, then the molecular areas of the non-ionic soaps (Table VIII) determined by equation [2] are all too high. The data in Table VIII were revised on the basis of a

molecular area for the oleate molecule at  $20.2 \text{ \AA}^2$  (Table X) rather than at  $28.2 \text{ \AA}^2$  to obtain the values in Table X.

TABLE X  
Molecular areas of non-ionic soap at titration end point by comparative soap adsorption (equation [2])

Comonomer	Bd in comonomer charge (%)	Emulsifier	C <sub>2</sub> H <sub>4</sub> O, units/molecule soap	Molecular area (Å <sup>2</sup> )
Styrene	72	Polyoxyethylene	30	116
		Nonyl phenol	20	89
		Polyoxyethylene	4	28.6
Styrene	50	Polyoxyethylene	20	78
		Nonyl phenol		
Acrylonitrile	66	Polyoxyethylene	30	103
		Nonyl phenol		
		Polyoxyethylene		
		Isopropyl phenol	5	19.8
		Polyoxyethylene	16	52

The best estimates for the anionic soaps in the mixed soap system are about  $8 \text{ \AA}^2$  for oleate, and about  $20 \text{ \AA}^2$  for Nacconol, less than those values obtained in systems where there is no soap interaction (Tables V, VI, VII). The decrease in the area of anionic soaps in the presence of non-ionic soaps may be attributed to the absence of electrostatic repulsion forces between anions and neighboring neutral non-ionic soap molecules. A plot of molecular areas (Table X) versus number of C<sub>2</sub>H<sub>4</sub>O units/soap molecule is shown in Fig. 2. The linearity of the relation indicates that the area per ethylene oxide unit is constant. This constancy is consistent with an orientation of the ethylene

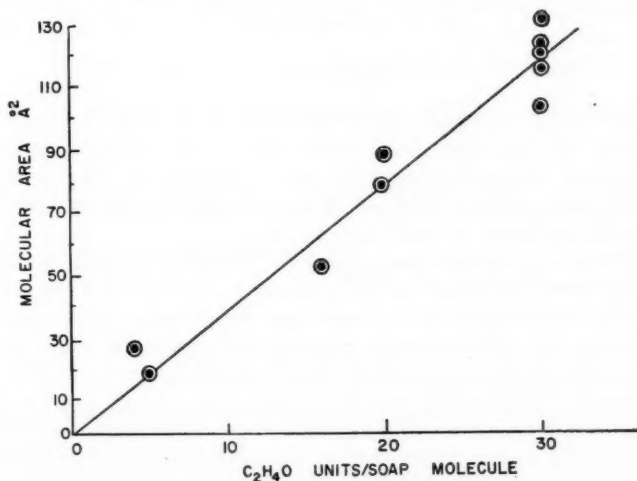


FIG. 2. Variation in area with ethylene oxide content.

oxide chain which is folded over the surface in a caterpillarlike manner. Such a view is supported by the results of Rosch (18), who suggested that chain contraction in polyethylene oxide chains is caused by the electrostatic attraction of the dipoles formed along the ethylene oxide chain. The actual dimensions of each fold may be determined only if the degree of hydration is known since the height of the fold should increase with increasing hydration. The work of Greenwald and Brown (19), showing a relation between salt content, temperature, and degree of hydration, suggests that measurements of area as a function of salt content would be instructive.

A set of dimensions was calculated for the unhydrated molecule from projections of Fischer-Hirschfelder models and the schematic representation in Fig. 3 was derived in which each fold is 16 Å high and contains 9 ethylene oxide units.



FIG. 3. Diagram of ethylene oxide chain at latex particle surface.

#### *Comparison of Behavior at Air-Water and Polymer-Water Surface*

Van Voorst Vader (20) has studied molecular areas of non-ionic and anionic soaps at the air-water interface. Measurements were made of saturation adsorptions, defined by Van Voorst Vader as the area occupied by a soap molecule at soap concentrations, where this area became independent of bulk concentration.

When non-ionic and ionic soaps were mixed, the molecular area of the non-ionic was not changed. The molecular area of the ionic soap was found to increase when non-ionic was added. This was explained by the increased ease of hydration of the ionic soap. When two dissimilar groups are present in the adsorbed soap layer, the water molecules are believed to be oriented to a configuration more suitable for co-ordination with ionic soap. Greater ease of co-ordination should increase the molecular area, since it will tend to decrease the affinity of the soap for the surface. The results we observed at the surface of latex particles, where the molecular area of the ionic soap is found to decrease in the presence of non-ionic, differ from Van Voorst Vader's results. Comparison of the

molecular areas of non-ionic soaps at the surface of the latex particles with those at the surface of the air-water interphase shows that non-ionic soaps have a greater affinity for the latter interphase. It appears reasonable to attribute the differing behavior of the ionic soap at the two interfaces to the differing affinity of the non-ionic for the surface.

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#### APPENDIX

This treatment is adapted from a similar problem with carbon black (21). The volume of  $N$  spherical particles is

$$V = \frac{\pi}{6} \sum_{i=1}^N X_i^3 = \frac{\pi}{6} \sum_{i=1}^N (\bar{X} - \rho_i)^3 = \frac{\pi}{6} \sum_{i=1}^N (\bar{X}^3 - 3\bar{X}^2 \rho_i + 3\bar{X} \rho_i^2 - \rho_i^3)$$

where  $\bar{X}$  is the average particle diameter.

Now

$$\sum_{i=1}^N \rho_i^2 = N\sigma^2,$$

where  $\sigma$  is the standard deviation, and, for symmetrical distribution,

$$\sum_{i=1}^N \rho_i = 0 = \sum_{i=1}^N \rho_i^3.$$

Appropriate combination of the three preceding equations gives

$$V = \pi \frac{N}{6} (\bar{X}^3 + 3\bar{X}\sigma^2).$$

In a similar way, it can be shown that the area of  $N$  particles is

$$\pi N (\bar{X}^2 + \sigma^2).$$

The area/volume ratio is then

$$\frac{6}{\bar{X}} \frac{(\bar{X}^2 + \sigma^2)}{(\bar{X}^2 + 3\sigma^2)}.$$

The maximum error introduced by the assumption of symmetry was calculated as 3% from the most unsymmetrical distributions obtained.

# PROTON MAGNETIC RESONANCE MEASUREMENTS OF FORMAMIDE<sup>1</sup>

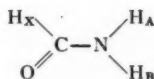
B. SUNNERS,<sup>2</sup> L. H. PIETTE, AND W. G. SCHNEIDER

## ABSTRACT

The high-resolution proton resonance spectrum of formamide has been measured and analyzed. Quadrupole broadening of the resonance signals due to the  $N^{14}$  nucleus was eliminated by substitution of the isotopic nucleus  $N^{15}$ . Twenty-four lines were resolved in the spectrum, which is consistent with restricted rotation about the C—N bond. The non-equivalence of the two protons in the  $NH_2$  group is characterized by a smaller screening constant and a greater spin-spin interaction of the proton which is in the *trans* position relative to the carbonyl group. It is suggested this difference in the spin coupling of the two protons may be associated with different N—H bond lengths. Pronounced changes in the chemical shifts and spin-coupling constants result when formamide is dissolved in dilute solution in water and acetone. In water solution the relative magnitudes of the spin coupling of the two protons in the  $NH_2$  group is reversed from that observed in pure formamide and the coupling of the aldehyde proton to  $N^{15}$  varies by nearly 50%. Heating of formamide above room temperature causes rotation of the  $NH_2$  group as well as proton exchange between neighboring molecules. The two effects could be separated. From the observed changes in the proton spectra as a function of temperature the barrier hindering rotation (measured in a 10 mole % solution of formamide in acetone) was found to be  $18 \pm 3$  kcal/mole. The activation energy for proton exchange in pure liquid formamide was found to be  $10 \pm 3$  kcal/mole.

## INTRODUCTION

Formamide is generally regarded as an approximately planar molecule. In the absence of free rotation about the C—N bond, the proton resonance spectrum may be expected to be of the type ABX (1) containing a minimum of 12 lines. Assuming the two protons on the nitrogen atom are only slightly non-equivalent the three protons may be labelled as follows:



The observed spectrum of ordinary formamide contains only a broadish doublet partially overlapped by a very broad signal arising from the  $NH_2$  group. The incomplete resolution and the broad nature of the lines derive from the quadrupole coupling of the  $N^{14}$  nucleus. This difficulty has been partially overcome by Piette, Ray, and Ogg (2) by use of the double-irradiation technique (3) to decouple the  $N^{14}$  nucleus. The resulting spectrum showed six lines of which four could be assigned to the "aldehyde" hydrogen and yielded the coupling constants corresponding to the spin interaction with the two protons in the amide group. The spectrum of the latter could not be completely resolved presumably because of incomplete saturation of the  $N^{14}$  nucleus. In the present work an alternative approach has been followed. Quadrupole broadening by  $N^{14}$  was eliminated by substitution of the nitrogen isotope  $N^{15}$ . Since this has spin  $I = \frac{1}{2}$ , sharp-line proton signals result, permitting a complete resolution and analysis of the spectrum as well as a study of proton exchange behavior and internal rotation about the C—N bond.

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<sup>2</sup>National Research Council Postdoctorate Fellow, 1957-59.



## EXPERIMENTAL

Two isotopically substituted compounds,  $\text{HCON}^{15}\text{H}_2$  and  $\text{DCON}^{15}\text{H}_2$ , prepared by Dr. L. Leitch, Pure Chemistry Division, National Research Council, were studied. The formamide- $\text{N}^{15}$  was prepared from ethyl formate and ammonia- $\text{N}^{15}$ , whereas the deuterated compound was similarly obtained from deuterated ethyl formate. The pure samples (containing at least 95%  $\text{N}^{15}$ ) were vacuum-distilled into 5-mm O.D. glass sample tubes, which were then sealed.

The proton resonance spectra were recorded at 40 Mc/s and at 60 Mc/s with a Varian V-4300 high-resolution spectrometer. Satisfactory resolution of the spectrum of the deuterated compound was obtained at both frequencies. However, the 40-Mc/s spectrum of the undeuterated compound was unsatisfactory for a complete analysis of the spectrum due to extensive overlapping of individual lines. The 60-Mc/s spectrum showed 20 (and in some cases 21) resolved lines out of the possible 24.\* Since the spectrum extended over a wide range ( $\sim 122$  cycles/sec), measurement of the more widely separated line spacings tend to be somewhat more inaccurate due to residual drift in the instrument. Where possible, some lines were checked by superposition of sidebands on the oscilloscope screen but most separations were obtained with the aid of sidebands recorded with the spectrum. A further check was provided by superposing a signal from another part of the spectrum on a given signal. This signal was then repeatedly traversed and recorded, the frequency being adjusted to maximize the signal. For well-resolved signals this procedure permits the determination of signal separation to an accuracy of about 0.1 cycle/sec.

## RESULTS

The proton resonance spectrum of  $\text{DCON}^{15}\text{H}_2$  recorded at 60 Mc/s is shown reproduced in Fig. 1. If the two protons on the nitrogen atom are non-equivalent, a simple four-line AB-type spectrum is to be expected. Each line of this spectrum would, however, have a large splitting due to spin coupling with  $\text{N}^{15}$ . It is apparent that the observed spectrum contains additional (triplet) splitting due to the deuterium atom ( $I = 1$ ), but this splitting is observable only on proton  $\text{H}_\text{B}$ , which is in the *trans* position relative to the deuterium atom. The value of the coupling constant,  $J_{\text{DB}}$ , is 2.1 cycles/sec. From the ratio of the nuclear gyromagnetic ratio of the proton and deuteron, the corresponding proton-proton coupling is calculated to be about 13.7 cycles/sec, in fair agreement with the value reported by Piette, Ray, and Ogg (2). This therefore identifies the signals of proton  $\text{H}_\text{B}$ , which appear at a higher field than those of proton  $\text{H}_\text{A}$ . With this assignment,† a complete analysis of the spectrum yields the chemical shift and spin-coupling constants shown in Table I.

An interesting feature of the above spectrum (cf. Fig. 1) is the noticeably larger separation of the  $\text{H}_\text{A}$  and  $\text{H}_\text{B}$  signals in the low-field half of the spectrum compared with those in the high-field half. The chemical shift,  $\nu_0\delta_{\text{AB}}$ , must of course be identical in both halves of the spectrum. It must be concluded therefore that the spin interaction

\*In a 10 mole % solution of  $\text{HCON}^{15}\text{H}_2$  in acetone all 24 lines of the spectrum could be resolved.

†As in reference 2, the assignment of signals in the spectrum to protons  $\text{H}_\text{A}$  and  $\text{H}_\text{B}$  is made on the assumption that *trans* coupling constants are much greater than *cis* coupling constants. This relationship of the coupling constants is well established for olefinic compounds (7, 8) and may be expected to hold also in formamide which is only slightly nonplanar. Moreover, the proton assignment arrived at on the basis of this assumption implies a slightly smaller shielding of the  $\text{H}_\text{A}$  proton compared with that of  $\text{H}_\text{B}$ , which is consistent with the order to be expected from the polar effects of the carbonyl group in the molecule (see below).

of proton  $H_A$  with the  $N^{15}$  nucleus is greater than that of  $H_B$ . The difference in the spin-coupling constants is about 4 cycles/sec.

TABLE I  
Proton chemical shifts\* and spin-coupling constants of formamide (in cycles/sec)

	$\begin{array}{c} \text{D} \\ \diagdown \\ \text{C}=\text{N}^{15} \\ \diagup \\ \text{O} \end{array} \begin{array}{c} \text{H}_A \\ \diagup \\ \text{H}_B \end{array}$	$\begin{array}{c} \text{H}_X \\ \diagdown \\ \text{C}=\text{N}^{15} \\ \diagup \\ \text{O} \end{array} \begin{array}{c} \text{H}_A \\ \diagup \\ \text{H}_B \end{array}$	8 mole % $\text{HCON}^{15}\text{H}_2$ in water	10 mole % $\text{HCON}^{15}\text{H}_2$ in acetone
$\nu_0\delta_{AB}$	12.1	12.0	20.5	12.8
$\nu_0\delta_{AX}$	—	-40.0	-25.3	-64.9
$J_{AB}$	2.5	2.4	2.3	2.9
$J_{AX}$	—	2.1	2.1	1.7
$J_{BX}$	—	12.9	13.6	13.5
$J_{DB}$	2.1	—	—	—
$J_{NA}$	91.6	92.0	91.9	91.0
$J_{NB}$	88.0	88.0	95.4	88.0
$J_{NX}$	—	19.0	23.3	16.4

\*At 60 Mc/s.

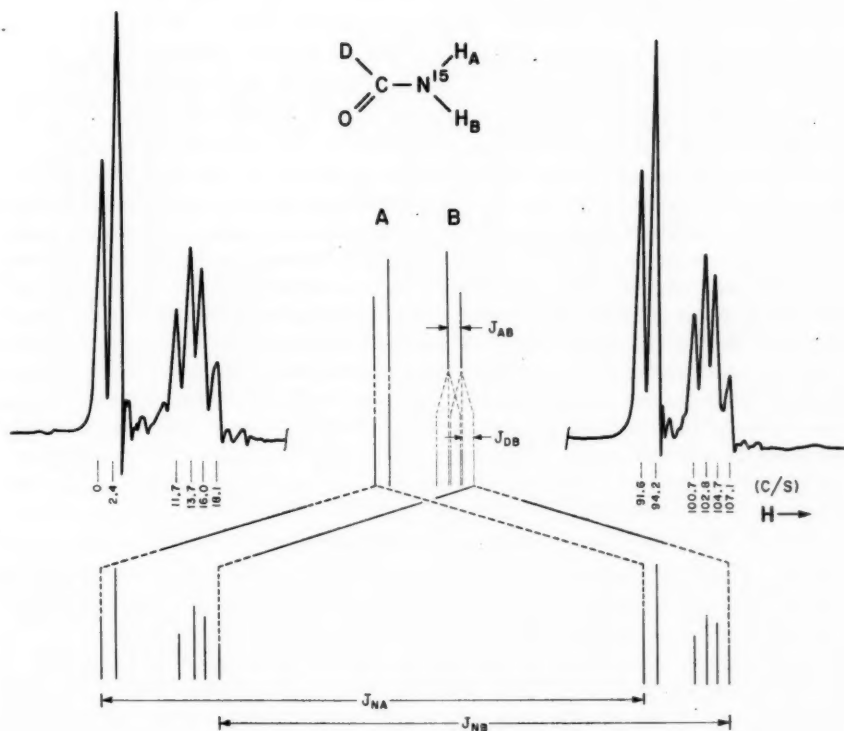


FIG. 1. Proton resonance spectrum of  $\text{DCON}^{15}\text{H}_2$  at 60 Mc/s.

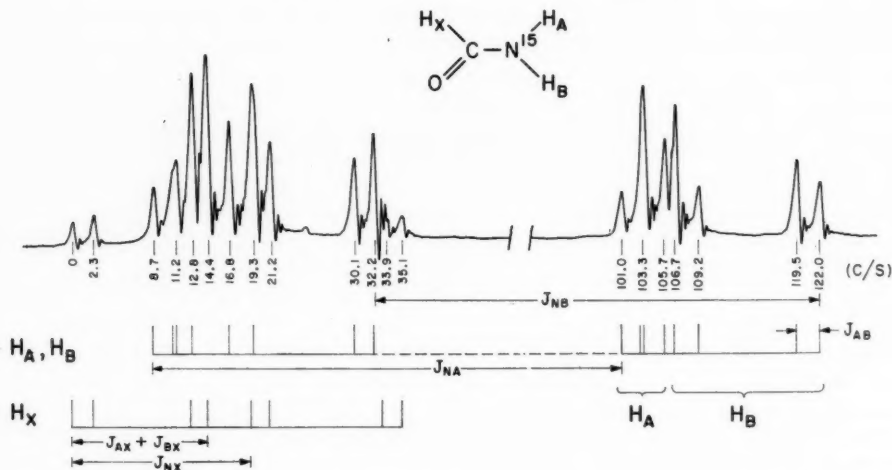


FIG. 2. Proton resonance spectrum of  $\text{HCON}^{15}\text{H}_2$  at 60 Mc/s. The assignment of lines is indicated schematically at the bottom of the spectrum.

Figure 2 shows the complete spectrum of  $\text{HCON}^{15}\text{H}_2$ , at 60 Mc/s. If each signal is split by  $\text{N}^{15}$  the spectrum should contain at least 24 lines. Of these, 20 are clearly resolved. Unfortunately the large splitting of protons  $\text{H}_\text{A}$  and  $\text{H}_\text{B}$  by the  $\text{N}^{15}$  nucleus causes half of the AB part of the spectrum to be superimposed on the X part of the spectrum ( $\text{H}_\text{X}$  signals). The latter shows a much smaller splitting by the  $\text{N}^{15}$  nucleus. The assignment of the spectrum is indicated in Fig. 2. The analysis of the spectrum was carried out on the basis of an ABXY system, where Y is the  $\text{N}^{15}$  nucleus, and assuming the coupling constants  $J_{\text{AY}}$  and  $J_{\text{BY}}$  (designated  $J_{\text{NA}}$  and  $J_{\text{NB}}$  in Table I) to be unequal. Since  $J_{\text{AY}}$  and  $J_{\text{BY}}$  are large, this leads to an effective "chemical shift" of the  $\text{H}_\text{A}$  and  $\text{H}_\text{B}$  nuclei in the low-field and in the high-field spectra of  $\nu_0\delta_{\text{AB}} + \frac{1}{2}(J_{\text{AY}} - J_{\text{BY}})$  and  $\nu_0\delta_{\text{AB}} - \frac{1}{2}(J_{\text{AY}} - J_{\text{BY}})$  respectively. The X spectrum consists of two sets of four lines. The outer members in each set are separated by  $(J_{\text{AX}} + J_{\text{BX}})$ , whereas the separation of the corresponding lines between the two sets is  $J_{\text{XY}}$  (indicated by  $J_{\text{NX}}$  in Fig. 2). The separation between the inner lines of the low-field quartet is  $2|A_+ - A_-|$  and that of the inner lines of the high-field quartet is  $2|B_+ - B_-|$ , where

$$[1] \quad A_{\pm} = \frac{1}{2} \left\{ [\nu_0\delta_{\text{AB}} + \frac{1}{2}(J_{\text{AY}} - J_{\text{BY}}) \pm \frac{1}{2}(J_{\text{AX}} - J_{\text{BX}})]^2 + J_{\text{AB}}^2 \right\}^{1/2},$$

$$[2] \quad B_{\pm} = \frac{1}{2} \left\{ [\nu_0\delta_{\text{AB}} - \frac{1}{2}(J_{\text{AY}} - J_{\text{BY}}) \pm \frac{1}{2}(J_{\text{AX}} - J_{\text{BX}})]^2 + J_{\text{AB}}^2 \right\}^{1/2}.$$

The results of the analysis are given in the third column of Table I. The estimated error in the chemical shifts and spin-coupling parameters is about  $\pm 0.15$  cycle/sec. It was not possible to determine relative signs of the spin-coupling constants.

The spin-coupling interaction of the  $\text{N}^{15}$  nucleus is again found to be greater with proton  $\text{H}_\text{A}$  than with proton  $\text{H}_\text{B}$ . This is a rather unexpected result if the two protons are symmetrically disposed with respect to the C—N bond axis. A very probable interpretation is, however, suggested by a recent structure determination of formamide by Costain and Dowling (4) from the microwave spectrum of the vapor, which showed the molecule to be nonplanar. The  $\text{NH}_2$  (amide) group was found to have a pyramidal

structure with a characteristic inversion frequency. Moreover the two N—H bonds have unequal lengths, that which is *trans* to the carbonyl group having a bond length of 1.000 Å while that of the other is 1.012 Å. This difference in bond lengths would seem to provide a simple explanation for the observed difference in the coupling constants  $J_{NA}$  and  $J_{NB}$  since it is reasonable to expect a greater spin-coupling interaction in the shorter bond.\*

The relative screening constants of protons  $H_A$  and  $H_B$  may also be expected to be affected by the difference in the N—H bond lengths and bond hybridization and to make the two protons non-equivalent. However, there are undoubtedly other contributing factors to the screening constants. In the first place the results show the proton  $H_A$  to be less screened (resonance at lower field) than  $H_B$ . This is not the relative order to be expected if the N— $H_A$  bond length is shorter than that of N— $H_B$ . In the liquid state the molecules are strongly hydrogen-bonded which could conceivably alter the degree of planarity of the molecule and the N—H bond lengths from those determined in the gaseous state, thus altering the relative screening constants (and possibly also the spin-coupling constants). The polar effect of the carbonyl group will also contribute to the screening constants of protons  $H_A$  and  $H_B$ . This contribution will tend to reduce the screening of proton  $H_A$  in the isolated molecule (5) and will become further enhanced in the liquid due to the "reaction" field of the surrounding molecules (6).

The present results confirm the large (six-fold) difference between the *cis* and *trans* proton-coupling constants in formamide. The observed values,  $J_{AX} = 2.1$  cycles/sec and  $J_{BX} = 12.9$  cycles/sec, are in good agreement with those reported by Piette, Ray, and Ogg (2). The relatively small value of  $J_{AB}$  (2.4 cycles/sec) is comparable to the small proton-proton coupling constants observed for the gem hydrogens of substituted ethylenes (7).

#### *Solutions of Formamide in Water and Acetone*

Proton resonance spectra of an 8 mole % solution of  $HCONH_2$  in water and of a 10 mole % solution in acetone were measured. The results are shown in Table I. Of particular interest are the changes in the chemical shifts and some of the spin-coupling constants compared with those observed in the pure liquid. All three systems are characterized by strong hydrogen-bonding interactions between the molecules and the observed changes in chemical shifts and spin-coupling constants must arise from the different nature of the interaction in the three systems. Changes in hydrogen-bonding interactions are known to produce large changes in proton chemical shifts, but ordinarily proton spin-coupling constants are not appreciably affected by such changes. In the present systems the spin-coupling constants show surprisingly large variations, amounting in one case,  $J_{NX}$ , to nearly 50%. Also for the water solution  $J_{NB}$  is increased by  $\sim 7$  cycles/sec and in this instance its magnitude exceeds that of  $J_{NA}$ , a reversal of the situation found in the other two systems. Such changes in the coupling constants, which are not well understood at present, may involve in the present example a change in the molecular geometry in addition to changes in molecular charge distributions. There are of course important differences in the nature of the hydrogen-bonding interactions in these systems. Thus in the acetone solution it may be supposed that the protons of the  $NH_2$

\*This difference in the two coupling constants may also be modified to some extent by small differences in bond hybridization (see, for example, Muller and Pritchard, *J. Chem. Phys.* **31**, 768 (1959) and Karplus and Grant, *Proc. Natl. Acad. Sci.* **45**, 1269 (1959)). The bond angles  $\angle CNH_A$  and  $\angle CNH_B$  are respectively  $120^\circ 17'$  and  $117^\circ 11'$  with the  $\angle H_A NH_B$  being  $119^\circ 22'$  (ref. 4). Thus if the N— $H_A$  bond has a slightly greater s-character than the N— $H_B$  bond this could contribute to making  $J_{NA}$  slightly greater than  $J_{NB}$ . We are indebted to a referee for pointing out this possibility.

group are strongly bonded to the acetone carbonyl group, leaving the carbonyl group in the formamide molecule itself relatively free. However, in a dilute solution in water the carbonyl group will be monopolized by the water protons, leaving the  $\text{NH}_2$  protons to be bonded to the oxygen atoms of neighboring water molecules. The proton resonance spectrum of the water solution at room temperature showed no evidence of proton exchange of the amide protons.

#### *Hindered Internal Rotation and Proton Exchange in Formamide*

By analogy with dimethyl formamide, which has a relatively high barrier hindering rotation about the C—N bond (9, 10), an observable hindered rotation of the  $\text{NH}_2$  group in formamide may be expected. The onset of the rotation will be characterized by a broadening and ultimate coalescence of lines in the proton spectrum. This does in fact occur when the pure compound is heated above room temperature. It is possible to demonstrate, however, that proton exchange involving the  $\text{NH}_2$  groups also sets in and contributes to the observed signal broadening and coalescence. Proton exchange can be satisfactorily eliminated over the required temperature range by working with a dilute solution of formamide in acetone. Under these conditions the formamide molecules are relatively isolated from each other and are hydrogen-bonded to the acetone with which they cannot exchange.

In order to measure the barrier hindering rotation of the  $\text{NH}_2$  group the proton spectrum of a 10 mole % solution of formamide in acetone was recorded at intervals of 2 or 3° C as the solution was progressively heated above room temperature. A few illustrative traces are reproduced in Fig. 3. It may be noted that at 25° C all 24 lines of the spectrum are clearly resolved. By far the most striking changes which appear in the spectrum on raising the temperature are those that occur in the  $\text{H}_\text{X}$  spectrum, which consists of eight lines on the extreme left (low-field side) of the spectrum. As mentioned earlier these eight lines result from the  $\text{N}^{15}$  doubling of the ordinary four-line X spectrum (cf. Fig. 2). For the present purpose we need only consider the quartet at lowest field, i.e. the four lines on the extreme left of the spectrum in Fig. 3. The two outer lines in this quartet have the separation  $|J_{\text{AX}} + J_{\text{BX}}|$  while the two inner lines are separated by  $2|A_+ - A_-|$ , where  $A_+$  and  $A_-$  are given by equation [1]. It is apparent from Fig. 3 that as the temperature is raised and internal rotation sets in, the two outer lines remain sharp and unaltered in position whereas the two inner lines broaden and ultimately coalesce. When the rotation of the  $\text{NH}_2$  group becomes sufficiently rapid, the quantities  $\nu_0\delta_{\text{AB}}$ ,  $J_{\text{AB}}$ ,  $(J_{\text{AY}} - J_{\text{BY}})$ , and  $(J_{\text{AX}} - J_{\text{BX}})$  all average to zero, and therefore the quantities  $A_+$  and  $A_-$  (see eq. [1]) both become zero and the two inner lines must coalesce. However, the quantity  $|J_{\text{AX}} + J_{\text{BX}}|$  is unaffected and the two outer lines remain unchanged. This sequence of changes converts the quartet to a triplet, the central component being doubly degenerate and separated by  $\frac{1}{2}(J_{\text{AX}} + J_{\text{BX}})$  from the two outer lines. Thus the total formamide spectrum has been changed from one of type ABXY to one of type  $\text{A}_2\text{XY}$  by virtue of rapid rotation of the  $\text{NH}_2$  group. This fact suggests that even at 98° proton exchange is still relatively unimportant. If proton exchange were rapid the final spectrum would have consisted of a doublet for the  $\text{H}_\text{X}$  signals, resulting from the  $\text{N}^{15}$  splitting, and a single line for the  $\text{NH}_2$  group. It is apparent, however, that the traces at 75° and 98° in Fig. 3 have broader lines in the X spectrum which may be attributed to the onset of slow proton exchange at these higher temperatures. The progressive shift of the  $\text{H}_\text{A}$  and  $\text{H}_\text{B}$  signals toward higher field with increasing temperature results from increased dissociation of the hydrogen bonds formed by these hydrogens with the acetone solvent.

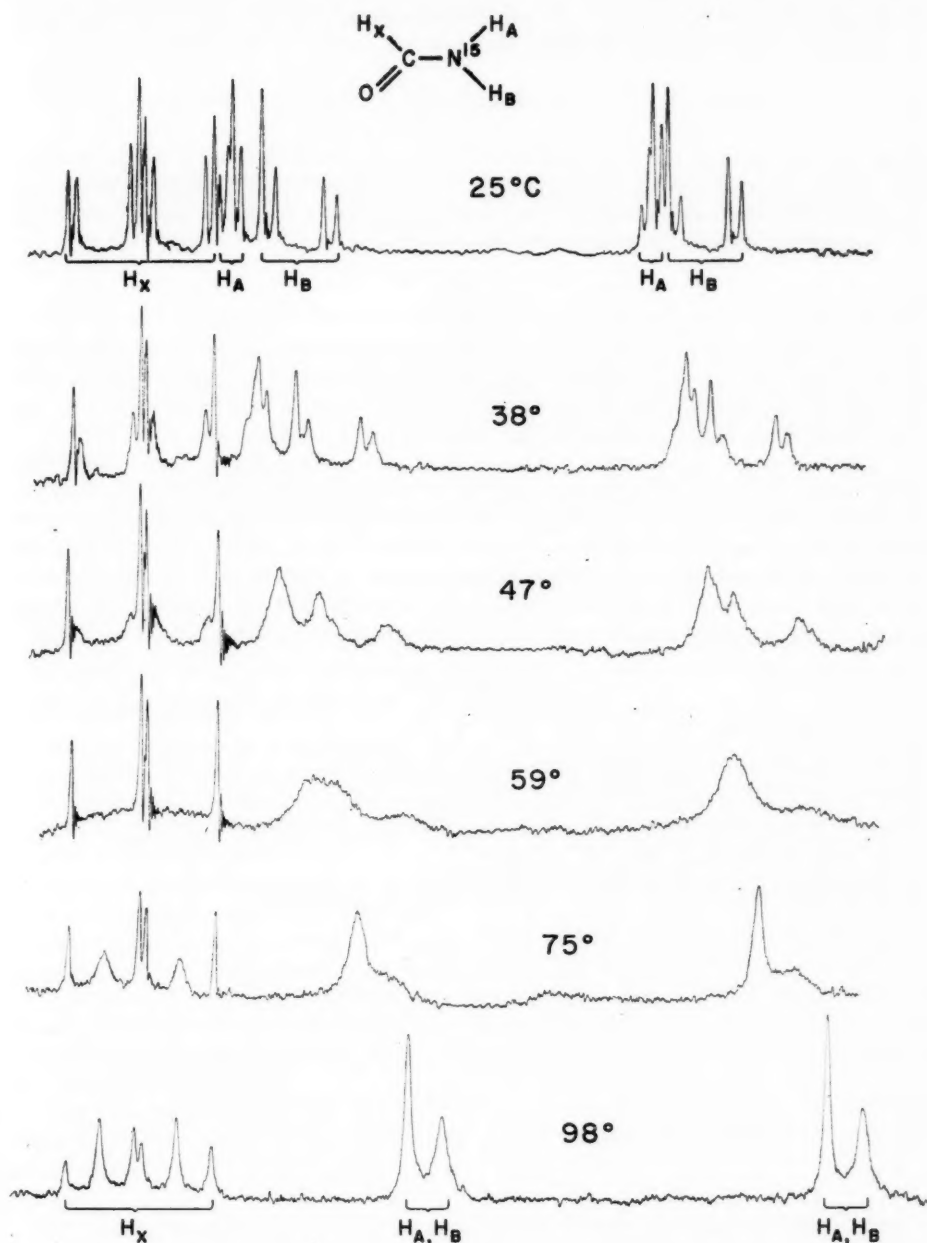


FIG. 3. Proton magnetic resonance spectrum of 10 mole % solution of  $\text{HCONH}_2$  in acetone at various temperatures showing signal broadening and coalescence due to hindered rotation of the  $\text{NH}_2$  group.



In order to evaluate the potential barrier hindering rotation, the lifetimes,  $\tau$ , of the protons at positions  $H_A$  and  $H_B$  were evaluated from the broadening of the lines in the X spectrum from the simple relation

$$[3] \quad \frac{1}{\tau} = \frac{1}{T'_2} - \frac{1}{T_2}$$

where  $1/T'_2$  is taken as the half-band width of the broadened line and  $1/T_2$  the effective line width in the absence of rotational broadening. The latter could be conveniently measured from the outer (unbroadened) lines in the X spectrum. To extend the range of observable  $\tau$  values the additional relation (10)

$$[4] \quad \tau = \frac{\sqrt{2}}{2\pi\Delta\nu}$$

was employed. Here  $\Delta\nu$  (in cycles/sec) is the separation of appropriate spin multiplet peaks in the AB spectrum whose coalescence is observed. The data employed were obtained in the temperature range of 25° to 62° C. From a plot of  $\ln \tau$  vs.  $1/T$  the mean value of the rotational barrier was found to be  $18 \pm 3$  kcal/mole.

Proton exchange measurements were carried out on samples of pure formamide rather than on the acetone solution. At higher temperatures, where internal rotation is already rapid, a further broadening and signal coalescence results from the onset of rapid proton exchange. Values of  $\tau$  were evaluated with the aid of the relations given in equations [3] and [4]. A somewhat greater scatter of individual  $\tau$  values compared with those obtained at lower temperatures was evident. The mean activation energy for proton exchange between formamide molecules was found to be  $10 \pm 3$  kcal/mole.

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# ELECTRON SPIN RESONANCE STUDIES OF THE RADIATION-INDUCED ADDITION OF HBr TO C<sub>2</sub>H<sub>4</sub> IN THE SOLID STATE<sup>1</sup>

F. W. MITCHELL,<sup>2</sup> B. C. GREEN, AND J. W. T. SPINKS

## ABSTRACT

Electron spin resonance measurements at 77° K have been used to study the hydrobromination of ethylene induced by  $\gamma$  irradiation of the solid mixture at liquid nitrogen temperatures. The evidence resulting from these studies has given valuable information regarding the reaction intermediates and has been used in formulating a likely reaction mechanism.

## INTRODUCTION

The addition of hydrogen bromide to ethylene under the influence of  $\gamma$  rays has been previously studied by Armstrong and Spinks (1, 2). The reaction is a chain reaction in the gas, liquid, and solid states; for example, with a dose rate of 450 r per minute, an initial  $G$  value of about  $10^5$  was found for additions in the liquid phase.  $G$  values in the solid phase were appreciably lower, particularly for long irradiations at liquid nitrogen temperatures.

A free radical chain reaction has been suggested for the reaction. The present work describes additional experiments, emphasizing e.s.r. techniques, bearing on the suggested mechanisms.

## EXPERIMENTAL

### *Purification of Materials*

Cylinder HBr and C<sub>2</sub>H<sub>4</sub> were passed through a P<sub>2</sub>O<sub>5</sub> drying tube and then subjected to a number of bulb-to-bulb distillations under high vacuum at liquid nitrogen temperatures. Both were finally distilled from a bath at -78° C.

### *Apparatus*

A general purpose high vacuum apparatus was used. After measurement the reactants were distilled into a simple reaction vessel constructed of 7-mm Pyrex tubing fitted with stopcock and joint. The volume of solid resulting from the usual amounts of reactants was very close to 0.5 ml.

Irradiations were conducted in a Dewar vessel of liquid nitrogen employing Co<sup>60</sup> sources of both 90 curies and 1100 curies.

Gas chromatographic studies were made using various columns and introducing the reaction products in the gaseous form. Column temperature control was available.

Electron spin resonance studies were made with a Varian V 4500 spectrometer. A cavity and Dewar were constructed to enable studies to be performed at 77° K. Some quantitative spin measurements were attempted using a range of DPPH solutions in dry benzene as standards.

Hyperfine splittings and line widths were determined by means of a Varian standard supplied by the manufacturers. Ferrous sulphate dosimetry was employed for dose rate estimations.

### *Results*

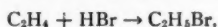
The normal experimental technique adopted was to mix the reactants after pressure measurements and condense them rapidly into the tip of the reaction vessel. After

<sup>1</sup>Manuscript received January 21, 1960.

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irradiation, the vessel was reattached to the vacuum line and allowed to warm up to room temperature. In agreement with the simple scheme,



equimolar amounts of reactants undergo a 50% pressure reduction for 100% addition (2). This does not preclude the formation of small amounts of other products, and accordingly the nature of the reaction products was further investigated by gas chromatography.

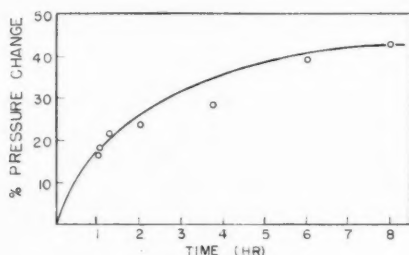


FIG. 1. Pressure change curve.

Figure 1 depicts the percentage pressure change plotted against time for single irradiations of equimolar solid mixtures. It can be seen that a 50% change could not be achieved (though stepwise irradiation of the same mixture with interim melting and cooling results in such a change). A 13-hour single irradiation gave a result slightly lower than that at 8 hours so that the limiting value of percentage of  $\Delta P$  may be taken as about 42%.

#### Gas Chromatography

Columns of dinonyl phthalate and silicone Hyvac grease on inert supports were used for the detection of products. Runs in which at least 80% addition had occurred were taken for analysis.

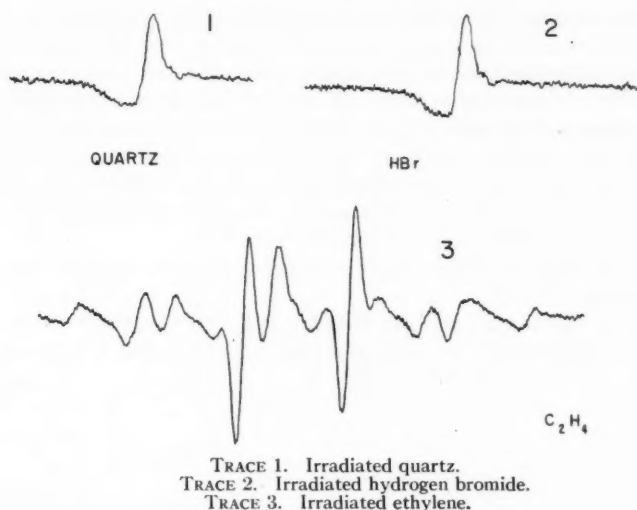
The principal product was clearly ethyl bromide, which had a retention time of 16 minutes at room temperature in a 4-ft DNP column. GLC revealed that attempts to separate mixtures of HBr,  $\text{C}_2\text{H}_4$ , and  $\text{C}_2\text{H}_5\text{Br}$  by fractionation at  $-120^\circ\text{C}$  had been unsatisfactory.

Of interest was the appearance of unknown peaks after 2 minutes at  $26^\circ\text{C}$  on the DNP column and 16 minutes at  $50^\circ\text{C}$  on the silicone column. Quantitative measurements based on relative peak areas indicated both to be present in a ratio of about 1:4000 compared with the amount of ethyl bromide. A sample of ethylene dibromide was taken and shown to have a retention time identical with that of one of the unknown peaks (16-minute one). The other unknown has a retention time suggesting that it is butene-1.

#### Electron Spin Resonance Studies

Samples of  $\text{C}_2\text{H}_4$ , HBr,  $\text{C}_2\text{H}_5\text{Br}$ , and  $\text{C}_2\text{H}_4\text{-HBr}$  mixtures were irradiated at  $77^\circ\text{K}$  in a 1100-curie cobalt-60 unit in 5-mm quartz tubing. Previous to irradiation, they were measured and degassed on the vacuum line. The dose rate for all samples was 1545 r per minute, or  $8.42 \times 10^{16}$  ev/g per minute.

The samples which had been irradiated in the dark were then transferred within 1 second to a specially constructed light-tight Dewar vessel, containing liquid nitrogen,



the tip of which extended into the spectrometer cavity. Some examples of the traces obtained are given.

*Trace 1* depicts the thermoluminescence peak arising from an evacuated quartz blank which had been given a dose of  $9.26 \times 10^5$  r. The entire quartz trace was found to disappear on warming to room temperature. Bleaching with tungsten light at 77° K resulted in an almost complete disappearance of the trace.

*Trace 2* arises from 118 cc NTP of HBr at identical spectrometer settings with trace 1 and results from the same dose, i.e.,  $9.26 \times 10^5$  r. No evidence of radical absorption from the sample can be seen. More extensive investigation revealed absorption due to the presence of H atoms but not due to anything else.

*Trace 3* was obtained from 118 cc NTP of C<sub>2</sub>H<sub>4</sub>. On integration and correction for the central thermoluminescence peak (due to the quartz, i.e., trace 1), the corrected absorption curve is as in Fig. 2. The outside line separation was 145.2 gauss and the quartet

C<sub>2</sub>H<sub>4</sub> ABSORPTION CURVE

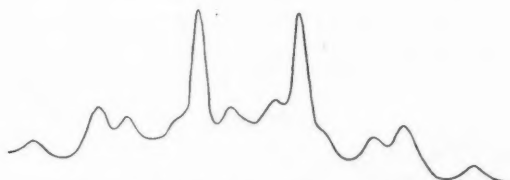


FIG. 2. True ethylene absorption curve (corrected).

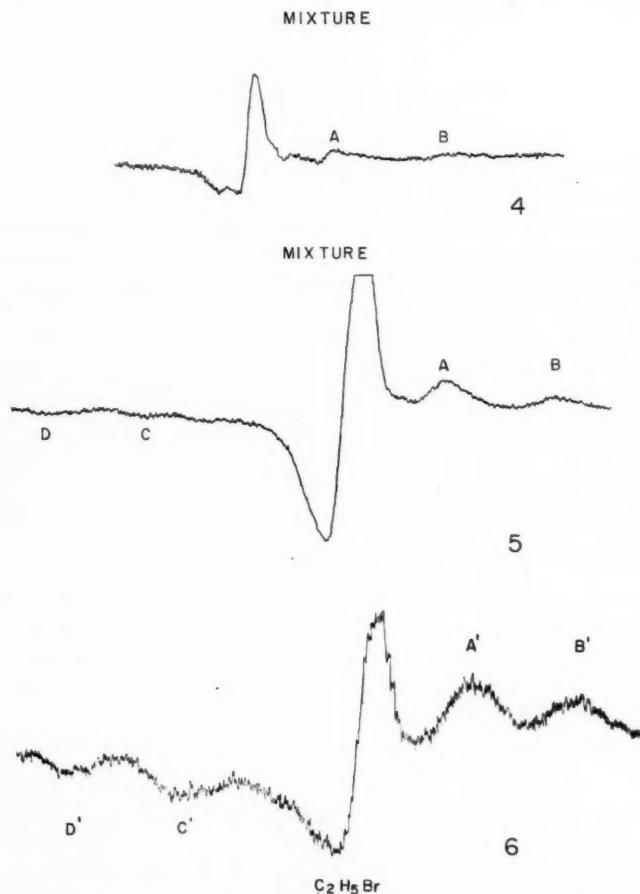
separation 87 gauss, the average separation between the quartet peaks being 29 gauss. This appears to correspond well with the quartet of triplets reported by Smaller and Matheson (3), resulting from the  $\gamma$  irradiation of ethane, ethylene, and ethyl chloride (quartet separation 79 gauss).

The number of ethylene molecules present was  $3.18 \times 10^{21}$ . Comparison of trace 3 with a standard DPPH sample in dry benzene indicated that there were  $5.4 \times 10^{16}$  spins present. If the trace arises from ethyl radicals, this indicates their concentration to be about 1 in  $5 \times 10^4$  of the ethylene molecules present. The total dose was  $9.26 \times 10^5$  r or  $0.85 \times 10^{19}$  ev. Assuming no ethyl radical decay, this gave a *G* value for their formation of 0.63.

Trace 4 was obtained from a mixture of 59 cc  $C_2H_4$  and 59 cc HBr given a dose of  $9.26 \times 10^5$  r. All evidence of ethyl radicals arising in trace 3 was absent. The small 'peaks' at A and B arise from radical structure but are very weak.

Traces 1-4 were made at identical power and spectrometer settings and, as such, are directly comparable.

Trace 5 arises at higher gain settings than trace 4 and brings out the peaks A and B more clearly. An unsuccessful attempt was made to split peak A into hyperfine lines.



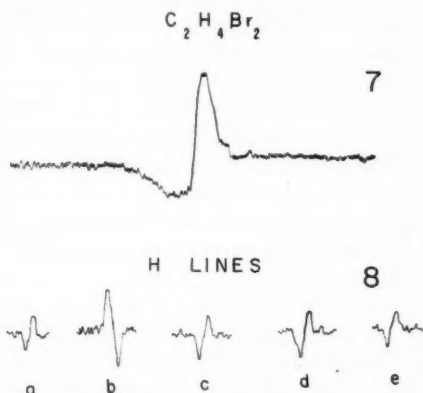
TRACE 4. Irradiated equimolar ethylene - hydrogen bromide mixture.

TRACE 5. As trace 4; higher spectrometer settings.

TRACE 6. Irradiated ethyl bromide.

Further very weak "peaks" at C and D appear to be present in this trace. The splitting from A to C is 81.6 gauss and from A to B 30.5 gauss.

Trace 6 arises from a sample of ethyl bromide which was degassed, sealed under vacuum, and given a dose of  $4.63 \times 10^5$  r, i.e., half that of the other samples. The positions of A', B', C', and D' are identical with those of A, B, C, and D in trace 5. The difference in appearance arises, no doubt, from differing amounts of radicals, but it appears likely that the same radical species is involved in both cases.



TRACE 7. Irradiated 1,2-dibromoethane.  
TRACE 8. H lines: (a) quartz, (b)  $C_2H_4$ , (c)  $HBr$ , (d)  $C_2H_4-HBr$ , (e)  $C_2H_4Br_2$ .

Trace 7 was obtained from a sample of dibromoethane which had been degassed, sealed under vacuum, and given a dose of  $9.26 \times 10^5$  r. Surprisingly, no trace of radical structure was observable, and the trace is identical with that arising from quartz treated similarly.

Trace 8 illustrates the high field H lines from (a) a quartz blank, (b) 118 cc NTP  $C_2H_4$ , (c) 118 cc NTP  $HBr$ , (d) 118 cc NTP equimolar  $C_2H_4-HBr$  mixture, (e) dibromoethane treated as described above. It can be tentatively inferred that the H atom concentration was highest in the ethylene samples, although the unexpected H line resulting from an evacuated quartz blank makes it impossible to ascertain from trace 8 whether H atoms are present in samples other than ethylene. Comparison with a standard sample of DPPH in benzene suggested that the H atom concentration in ethylene was a factor of the order of  $10^3$  lower than the ethyl radical concentration in the same sample. This is in partial disagreement with Matheson (3), who did not find any H atom doublet for ethylene but did find that at  $77^\circ K$  the hydrogen atom doublet for irradiated ethane was relatively weak compared with the ethyl radical trace.

#### DISCUSSION

The foregoing work helps to clarify the reaction mechanism suggested by Armstrong and Spinks (1). The presence of small amounts of ethylene dibromide among the end products suggests the reaction:



as a main termination reaction. The presence of butene-1, if confirmed, would possibly indicate the reaction





The main evidence of interest stems from the e.s.r. work which indicates that ethyl radicals result from the irradiation of ethylene and that H atoms result from the irradiation of ethylene. Of great interest is the fact that irradiation of  $C_2H_4-HBr$  mixtures shows no measurable trace due to ethyl radicals, indicating that the  $C_2H_5$  radical reacts very rapidly even at liquid nitrogen temperatures. That the radical species present in a  $C_2H_4-HBr$  mixture and  $C_2H_5Br$  after irradiation should be identical (traces 5 and 6) is also of extreme interest and could possibly be taken to indicate that the chain reaction had already occurred before warming. However, the difficulty of diffusion of large radicals such as  $C_2H_4Br$  in the mixture and the energy requirements of the chain propagating steps would make this unlikely at  $77^\circ K$ . A more satisfactory suggestion would be that the radical species involved is  $C_2H_4Br$ , which would be the most likely radiation product of  $C_2H_5Br$  and which could arise in  $C_2H_4-HBr$  mixtures at  $77^\circ K$  in the manner indicated below. Nothing is known of the e.s.r. structure of such a radical at present, but the presence of a bromine isotope with a nuclear spin of  $3/2$  would undoubtedly make it complex.

As has been mentioned above, an extensive examination of the trace resulting from irradiated HBr revealed no absorption other than that arising from the quartz sample tube. It would also be difficult to state that the hydrogen line arising in trace 8 resulted from any higher concentration of hydrogen atoms than was present in the quartz blank. Bromine atoms, if present, would be paramagnetic and give rise to e.s.r. absorption. It would thus appear likely that neither hydrogen nor bromine atoms produced in the primary radiation processes had escaped recombination. The following series of reactions were proposed by Zubler, Hamill, and Williams (4) to be consistent with their studies on the X radiolysis of HBr.



In the solid phase at  $77^\circ K$  the above mechanism is a likely one, and dissociative electron capture by the parent ion will be of increased importance.



The  $\gamma$  irradiation of pure ethylene might be expected to occur as follows:



Again reaction [9a] is a more likely one in the solid phase. The charge transfer reaction [10] which was proposed by Field *et al.* (5) in the electron radiolysis of ethylene can doubtless result in other alternative products.

The e.s.r. studies (traces 3 and 8) strongly suggest that the only radical species present is the ethyl radical and that H atoms are present in the solid phase before warming. Ethyl radicals could arise from the reaction,



which is likely to have a very low activation energy (6) and which has been shown to occur at liquid air temperatures (7). This mechanism receives strong support from recent work (12, 13) which has indicated that hydrogen atoms readily add to olefins at 77° K to produce alkyl radicals in a manner which is likely to result in their stabilization in the matrix.

If reaction [9b] is the chief source of hydrogen atoms, the ethylenyl radical,  $C_2H_3$ , presumably disappears by some radical combination reaction such as (2).

In the irradiation of ethylene-hydrogen bromide mixtures energy transfer processes can readily occur.



Ethylene, having a ground state containing a considerable number of states of higher multiplicity than the singlet, is a particularly effective quencher (8).

Traces 4 and 5 indicate that the ethyl radicals arising in the irradiation of pure ethylene are not present in the mixture at 77° K. A simple explanation of their disappearance would be the occurrence of the combination reaction,



which is likely to have zero activation energy.

Alternatively, the ethyl radical might disappear by the hydrogen abstraction reaction



This has been calculated to have a low activation energy (2 kcal) by Anderson *et al.* (9). The presence of excited HBr molecules would enhance the likelihood of reaction [13b].

The identical nature of the radical species present in ethyl bromide and the mixture (traces 5 and 6) might very well be due to the presence of the  $C_2H_4Br$  radical, which is the most probable common radiation product of the two systems at 77° K.

Quantitative observations based on DPPH standards suggest that the number of radical spins in the irradiated mixture is very much less than  $5.4 \times 10^{16}$ , which is the calculated value for the ethyl radicals in trace 3.

Vaughan *et al.* (10) proposed a chain mechanism for the photo-addition of hydrogen bromide to ethylene in which the propagating steps were



It is most probable that the same propagating mechanism is involved in the radiation-induced addition being studied here and the occurrence of reaction [14] at 77° K could obviously account for the presence of  $C_2H_4Br$  radicals in the mixture before warming. The activation energy for this reaction has been shown to be zero from studies on the photobromination of ethylene (11).

Evidence exists to show that ethylene and hydrogen bromide form a loose compound ( $C_2H_4 \cdot HBr$ ) on condensing the mixture in the solid phase. Thus, the occurrence of the ionization and electron capture reactions [8] and [4], respectively, might well, as a result of proximity, favor the charge neutralization process



which, therefore, would be an alternative source of  $C_2H_4Br$  radicals.

Termination of the reaction chain can occur in a number of ways as suggested by Armstrong and Spinks in reactions [17] to [20b] of their paper (1).

The nature of the radical species present in irradiated ethyl bromide and  $C_2H_4$ -HBr mixtures together with other alkyl halides, and the reasons for the somewhat abnormal appearance of their e.s.r. traces are being further investigated. Temperature control above  $77^\circ K$  of samples examined by e.s.r. techniques would obviously be very informative with regard to the warm-up of the irradiated solid mixture.

#### ACKNOWLEDGMENTS

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# POTASSIUM DERIVATIVES OF FLUORENE AS INTERMEDIATES IN THE PREPARATION OF C<sub>9</sub>-SUBSTITUTED FLUORENES

## I. THE PREPARATION OF 9-FLUORENYL POTASSIUM AND THE INFRARED SPECTRA OF FLUORENE AND SOME C<sub>9</sub>-SUBSTITUTED FLUORENES<sup>1</sup>

G. W. H. SCHERF AND R. K. BROWN

### ABSTRACT

9-Fluorenylpotassium and 9,9-fluorenyldipotassium have been prepared from the reaction of potassium metal with fluorene in dioxane. These organometallic compounds upon reaction with alkyl and aralkyl halides gave 9-substituted fluorenes.

Six different absorption bands in the spectrum of fluorene could be associated with the methylene group: 2930, 1400, 1298, 952, and 692 cm<sup>-1</sup>. Evidence for this assignment was obtained from deuteration of the organometallic compounds of fluorene and from 9-substituted fluorenes.

### INTRODUCTION

During a study of the reactions of certain substances with fluorene it was found desirable to have at hand direct and relatively simple methods for the preparation of C<sub>9</sub>-mono- and C<sub>9</sub>-di-substituted fluorenes uncomplicated by contaminating side reactions due to addition of bases (1) usually required to effect reaction at the methylene group. In addition, quite indispensable would be a reliable and rapid method for distinguishing between mono- and di-substitution at C<sub>9</sub>, which would thus simplify the assessment of mixtures of 9-mono- and 9-di-substituted fluorenes and permit the investigator to follow more conveniently the separation of such mixtures. It was thought that monovalent metal "salts" of fluorene might lend themselves readily to the attainment of the first goal, while infrared spectroscopy should be most admirably suited to the second. Both the literature evaluation and the experiments described in this report show that this is indeed the case.

### 9-SUBSTITUTED FLUORENES FROM 9-FLUORENYSODIUM AND 9,9-FLUORENYLDIPOTASSIUM

Synthesis of C<sub>9</sub>-substituted fluorenes has been reviewed by Rieveschl and Ray (2). Generally, alkaline conditions promote the transient formation of the 9-fluorenyl carbanion which then by nucleophilic attack upon compounds of suitable structure produces the desired structure (2, 3). Equimolar proportions of fluorene, base, and substrate are expected to form 9-monosubstituted fluorenes, but there are reports which show that di- rather than mono-substitution has in fact occurred (4).

The formation of 9-fluorenylsodium by direct reactions between fluorene and metallic sodium, although reported in the patent literature, has been found highly unsatisfactory both in this laboratory and by other workers (3). However, Greenhow *et al.* describe the preparation of 9-fluorenylsodium in good yield by the reaction of sodamide with fluorene in boiling decalin (3). Through this organometallic compound the C<sub>9</sub>-monosubstituted fluorenes are accessible (3, 5-8). Indirect preparation of 9-fluorenylsodium via interchange with triphenylmethyl sodium (9) and, more conveniently, of 9-fluorenyllithium from alkyllithium compounds (10, 11) provide other routes, though somewhat more complicated, to the preparation of 9-substituted fluorenes. The Grignard reagent, 9-fluorenyl-

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Contribution from the Department of Chemistry, University of Alberta, Edmonton, Alberta.

magnesium bromide, is reported to lead to monosubstitution at C<sub>9</sub>, but reactions leading to dimeric products occur in some of the cases studied (10).

We have repeated the preparation of 9-fluorenylsodium according to Greenhow (3) and although the reported high yields and fine quality of the organometallic compound could not be duplicated, the salt was obtained in reasonable yield and in a state suitable for the synthesis of the 9-monosubstituted fluorenes as described by Greenhow and co-workers (3, 5). The 9-methyl-, 9-allyl-, and 9-benzyl-fluorenes required for this work were made by this method.

The 9,9-disubstituted fluorenes were readily obtained from 9,9-fluorenyldipotassium. Little work appears in the literature concerning the potassium salt of fluorene. Weissgerber (12) reported the preparation of 9-fluorenylpotassium by fusion of solid potassium hydroxide with fluorene at 280° from which was isolated a substance whose analysis indicated the composition C<sub>13</sub>H<sub>9</sub>K. This substance he then treated with benzyl chloride to form the 9-benzylfluorene. However, as Thiele and Henle have shown (13), the compound actually obtained was 9,9-dibenzylfluorene. A repetition of Weissgerber's experiment led to the conclusion that this method for the preparation of fluorenylpotassium also was quite unsatisfactory for our purpose.

It was found in this laboratory that potassium metal reacts readily with fluorene in boiling dioxane, protected by an atmosphere of nitrogen, to produce at will either the mono- or di-potassium salt as a reddish-brown precipitate. Hydrogen gas is evolved. This precipitate can be freed of unreacted fluorene by filtration and washing with dry hexane. The monopotassium derivative, obtained by the reaction of equimolar proportions of potassium and fluorene, can be isolated under nitrogen as a solid\* quite suitable for further reaction. Usually it is more convenient to leave the solid suspended either in the original dioxane, or in the hexane wash liquid where it can be kept for some time with little decomposition. Exposure to air causes rapid decomposition to a dark mass which is essentially potassium hydroxide, 9-fluorenone, 9-fluorenol, and fluorene, the relative amounts of these depending upon the accessibility to oxygen or water of the air. Attempts to analyze the isolated monopotassium salt gave low values for potassium presumably due to absorption of water and/or oxygen from the air during weighing manipulations. Three analyses gave an average value of 15.3% of potassium. The theoretical value is 19.15%. It was felt that the highly elaborate procedure obviously necessary for a satisfactory potassium analysis was superfluous to our work at this time hence further attempts in this direction were abandoned.

The dipotassium compound, precipitated from the reaction of one equivalent of fluorene with two of potassium, could not be isolated readily as above, and therefore was used in dioxane suspension immediately following its preparation. That we were actually dealing with the dipotassium compound was supported by (a) the fact that *two* equivalents of potassium metal were totally consumed by *one* equivalent of fluorene whereas potassium metal itself showed no visible reaction when heated alone with dioxane over a period of 8 hours, (b) the infrared spectrum of dideuterated fluorene (described later) obtained from the dipotassium compound, and (c) the nuclear magnetic resonance analyses for deuterium† which showed the absence of any peak corresponding to the methylene group of fluorene. On the other hand, the monopotassium compound, when deuterated, showed strong evidence from the infrared spectra that essentially 9-mono-deuterofluorene had been obtained, contaminated with a small amount of unreacted

\*The presence of particles of unreacted potassium accelerates the decomposition of the organometallic compound hence it is advisable to carry the reaction to completion with respect to the metal.

†The deuterium analyses were made by Dr. W. Schneider of the National Research Council of Canada in Ottawa.



fluorene and some 9,9-dideuterofluorene. This is supported by the nuclear magnetic resonance spectra which indicate approximately 75% monodeuteration. Rather than postulate that the "9-fluorenylpotassium" contained fluorene and 9,9-fluorenyldipotassium (a condition highly unlikely due to the great reactivity of the dipotassium compound) the results can be better explained by assuming that in the presence of KOD and excess  $D_2O$ , during the preparation and isolation procedure, a hydrogen-deuterium exchange has occurred, thus producing some  $C_9$ -dideuterated fluorene.

The addition of slightly more than two equivalents of alkyl or aralkyl halide to the suspension of the dipotassium compound in dioxane produced 9,9-disubstituted fluorenes in yields of about 65%. No further attempts were made at this time to improve yields since the reactions of the metallated fluorenes will be elaborated in a subsequent publication. In this way 9,9-dimethyl-, 9,9-dibenzyl-, and 9,9-diallyl-fluorene were prepared.

Reaction of the mono- and di-potassium compounds, in dioxane, with excess deuterium oxide gave 9-monodeutero- and 9,9-dideutero-fluorene respectively.

#### THE INFRARED SPECTRA OF FLUORENE AND SOME OF ITS $C_9$ -MONO- AND $C_9$ -DI-SUBSTITUTED DERIVATIVES

The information concerning the infrared studies of fluorene and its 9-substituted derivatives is meager. Fox and Martin (14) in a study of the absorption in the  $3000\text{ cm}^{-1}$  region, due to the methylene group in a number of organic compounds, attributes two frequencies,  $2901\text{ cm}^{-1}$  and  $2795\text{ cm}^{-1}$ , to the  $=CH_2$  of fluorene. In the present work the spectra of fluorene determined in carbon tetrachloride did not reveal absorption at these two frequencies which could be associated with the methylene group in fluorene. Richards and Thomson (15), investigating the spectral changes occurring in liquid-solid state transitions give two frequencies,  $1303\text{ cm}^{-1}$  and  $1482\text{ cm}^{-1}$ , apparently characteristic of fluorene. Both of these frequencies are found in this work, that in the  $1300\text{ cm}^{-1}$  region is definitely associated with the  $CH_2$  group while the  $1482\text{ cm}^{-1}$  band appears to be due to some other part of the fluorene structure.

In this paper are reported the infrared spectra of the following compounds: fluorene, 9-mono- and di-deutero-, mono- and di-methyl-, mono- and di-benzyl-, mono- and di-allyl-fluorene as well as 9-benzylidenefluorene. They were found in both carbon disulphide and carbon tetrachloride solution to provide the whole range of absorption from  $4000\text{ cm}^{-1}$  to  $600\text{ cm}^{-1}$  except for a small region about  $1450\text{ cm}^{-1}$  to  $1600\text{ cm}^{-1}$  where both solvents show some absorption themselves (16). The instrument available was a Perkin-Elmer double-beam infrared spectrophotometer, equipped with a sodium chloride prism. Six frequencies of medium intensity were found definitely due to the methylene group of fluorene. These are at  $2930$ ,  $1400$ ,  $1298$ ,  $1190$ ,  $952$ , and  $692\text{ cm}^{-1}$  (Fig. 1). Whether these are all fundamental frequencies or not is not known. There are, no doubt, other frequencies due to the methylene group arising from overtones and combinations, but these were felt to be unnecessary for our work and hence not examined. Two such frequencies of low intensity might be  $867$  and  $853\text{ cm}^{-1}$  (Fig. 1). All six frequencies can be clearly discerned and are of approximately the same intensity in both solvents employed. Since additional frequencies associated with substituting groups appear in the  $1400$  to  $600\text{ cm}^{-1}$  region this area was examined carefully and thus only the spectra for this region, found in carbon disulphide, are reported and shown in Figs. 1 to 13. Each of the six frequencies mentioned is markedly affected by substitution or deuteration at  $C_9$ . In all cases, monosubstitution by an alkyl or aralkyl group greatly reduces or eliminates the absorption at these frequencies while disubstitution removes it completely. The removal of some is masked by neighboring frequencies or new frequencies due to the substituting groups but can still



be readily observed. Mono- and di-deuteration reduces or removes these frequencies similarly but new bands appear for the C—D functions at a lower frequency as expected (Figs. 2 and 3). The relative positions of these new C—D frequencies were estimated beforehand from Fig. 1 by using the suggested factor of 0.73 (16) and thus the new frequencies could be related at least tentatively, if not exactly, to the former C—H frequencies. The experimentally found ratio of the new C—D frequency to the original C—H frequency is approximately 0.7, in agreement with the shift expected by a simple application of Hooke's Law (16). The frequencies for the original C—H group, the new C—D group, the remaining C—H group on monodeuteration, and the ratio of the first two, both calculated and found, are shown in Table I.

TABLE I  
Frequencies associated with the methylene group in fluorene and in monodeuterofluorene ( $\text{cm}^{-1}$ )

Observed for $\text{CH}_2$	Calculated <sup>a</sup> for $\text{HC—D}$	Observed for $\text{HC—D}$	Observed $\frac{\nu\text{C—D}}{\nu\text{C—H}}$	Observed for remaining $\text{DC—H}$
692	505	— <sup>b</sup>	—	677
952	694	667	0.70	939
1190	869	827	0.70	— <sup>d</sup>
1298	947	939	0.72	— <sup>d</sup>
1400	1022	974	0.70	— <sup>d</sup>
2930	2050	2150 <sup>c</sup>	0.73	— <sup>d</sup>

<sup>a</sup>The product of the observed frequency in column 1. and the factor 0.73 obtained from reference 16.

<sup>b</sup>Beyond the range of the instrument.

<sup>c</sup>This is a very weak absorption and is not certain.

<sup>d</sup>Overlapping and multiplicity of neighboring absorption makes any assignment highly questionable.

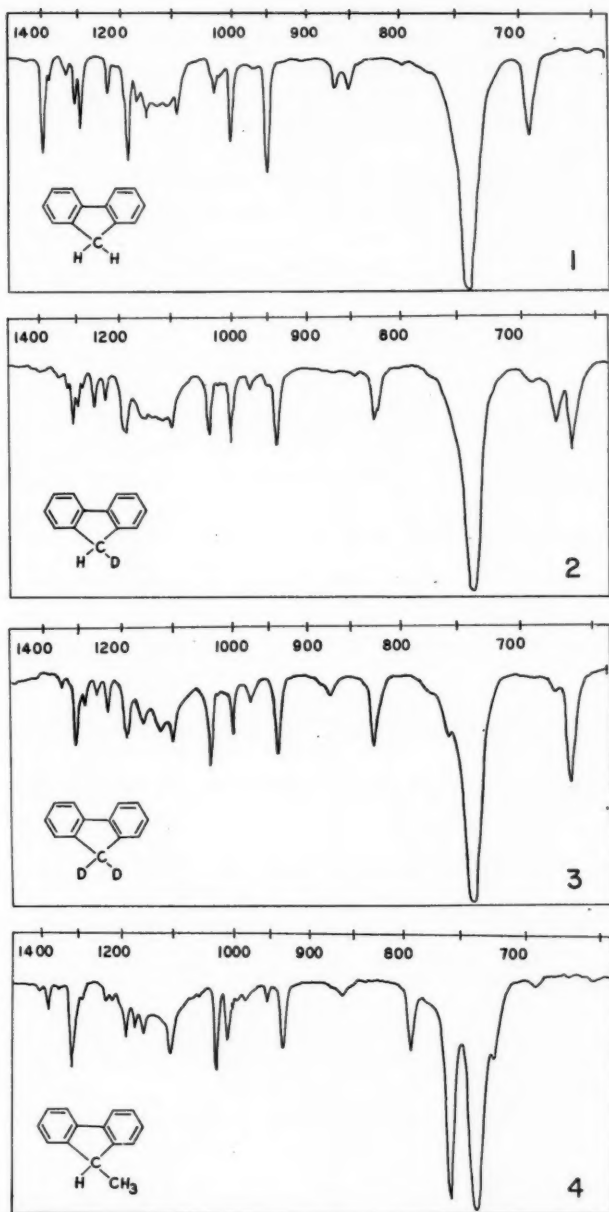
#### The 692 $\text{cm}^{-1}$ Band

This band, probably due to methylene rocking vibrations (16), is quite distinct. Monodeuteration (via the monopotassium compound) reduces it markedly (Fig. 2). The residual absorption noticeable at this frequency is most likely due to unreacted fluorene, a contaminant undoubtedly present since the deuterium oxide available at the time of these experiments contained 95% of  $\text{D}_2\text{O}$ . A three- to five-fold excess of deuterium oxide was used to ensure as complete a reaction as possible with the precipitated potassium compound. Purification by separation of deuterated from undeuterated fluorene obviously is extremely difficult. Dideuteration via the dipotassium compound completely eliminates the 692  $\text{cm}^{-1}$  band (Fig. 3). The spectrum of the monodeuterated fluorene shows a new

band at 677  $\text{cm}^{-1}$  which is thought to be associated with the remaining DC—H, shifted

from the original frequency of 692  $\text{cm}^{-1}$  by the presence of the deuterium atom. This point of view is supported by the fact that dideuteration reduces this 677  $\text{cm}^{-1}$  band to a very small value, this residual absorption arising, no doubt, from contaminating mono-

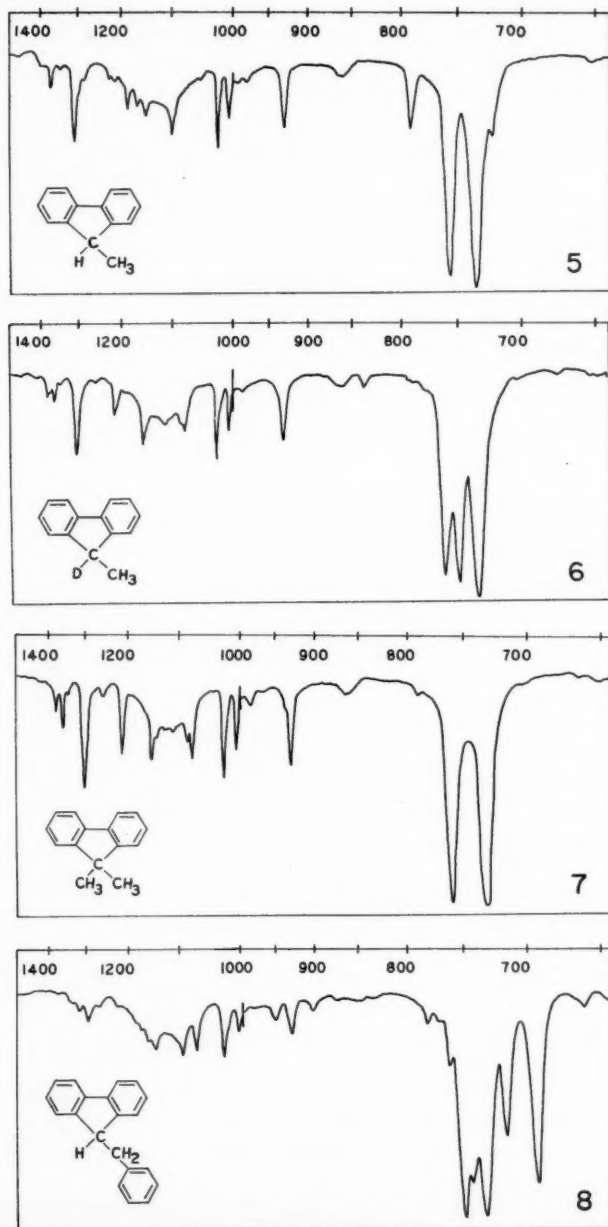
deuterated fluorene. The frequency corresponding to the new HCD— group, calculated to be in the region of 505  $\text{cm}^{-1}$ , is beyond the range studied.



FIGS. 1-4.

Monomethylation reduces the band at  $692\text{ cm}^{-1}$  to one of weak absorption at the same frequency (Fig. 4). This was found to be due to contamination by unreacted fluorene since repeated purification by chromatography on activated alumina eliminated the

absorption at  $692\text{ cm}^{-1}$  (Fig. 5). The melting point of the "contaminated" monomethylfluorene is  $43\text{--}44^\circ\text{C}$  whereas that of the "pure" monomethylfluorene is  $45\text{--}46^\circ\text{C}$ . Thus, a routine melting point determination of this compound should be carefully done to



FIGS. 5-8.

differentiate between 100% purity and slight contamination, sufficient to be visible clearly in the infrared spectrum.

The melting point found for 9-methylfluorene is the same as that reported by Greenhow (3). However, other workers give a melting point of 58° (17). This may be another example of two polymorphic forms, a situation already demonstrated in the case of 9,9-dimethylfluorene (18).

The disappearance of the 692  $\text{cm}^{-1}$  band on monobenylation and dibenylation (Figs. 8 and 9) is masked by the strong absorption at 697  $\text{cm}^{-1}$  due to out-of-plane C—H vibrations of monosubstituted benzene (16). Mono- and di-allylation (Figs. 11 and 12) show more clearly the disappearance of the 692  $\text{cm}^{-1}$  band.

The expected complete elimination of the 692  $\text{cm}^{-1}$  absorption in the 9-benzylidene-fluorene (Fig. 13) is obscured by the strong absorption at 697  $\text{cm}^{-1}$  due to monosubstituted benzene.

#### *The 952 $\text{cm}^{-1}$ Band*

This band whose origin is unknown to us is also quite distinct (Fig. 1). It is nearly eliminated by monodeuteration, the residual absorption most likely being due to contaminating fluorene (Fig. 2). Dideuteration causes complete disappearance of absorption

at this frequency. The corresponding HC—D band, calculated to occur in the region of 694  $\text{cm}^{-1}$  appears at 667  $\text{cm}^{-1}$  and its intensity increases markedly upon dideuteration.

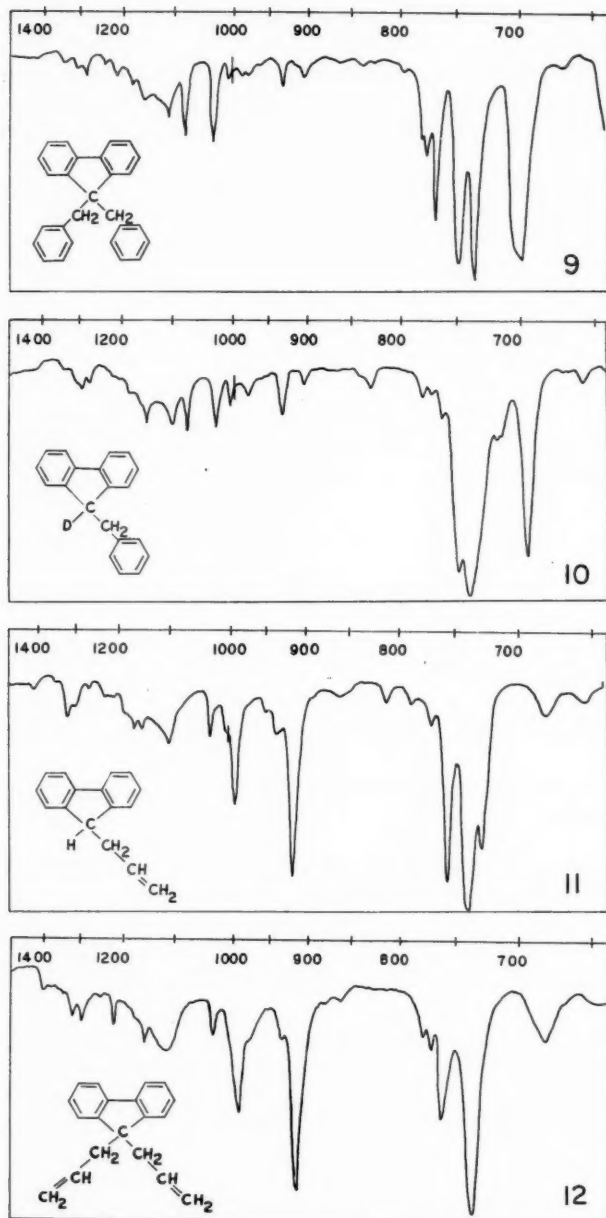
The considerably greater intensity of the HC—D band at 667  $\text{cm}^{-1}$  as compared to that of the DC—H band at 677  $\text{cm}^{-1}$  indicates that in deuteration of the monopotassium compound with excess  $\text{D}_2\text{O}$ , some dideuteration had occurred probably by hydrogen-deuterium exchange.

The band due to the remaining DC—H, if analogous to that of 677  $\text{cm}^{-1}$  found for the 692  $\text{cm}^{-1}$  band, should occur in the region of 935  $\text{cm}^{-1}$ . One actually does appear at 939  $\text{cm}^{-1}$  and may contain the DC—H absorption. However, the magnitude of its intensity as well as the fact that dideuteration makes no significant change in its size favors the view that the 939  $\text{cm}^{-1}$  band is due in part to the methylene absorption originally at 1298  $\text{cm}^{-1}$ , shifted due to formation of the —C—D bond, and in part to absorption from

the remaining —C—H bond affected by the deuterium atom.

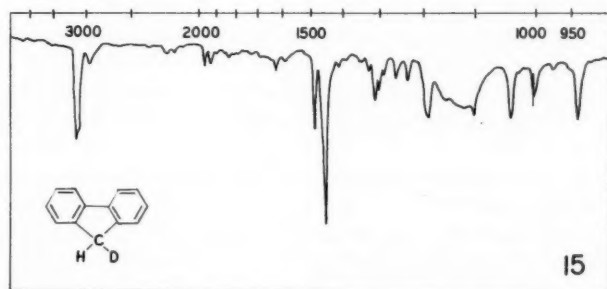
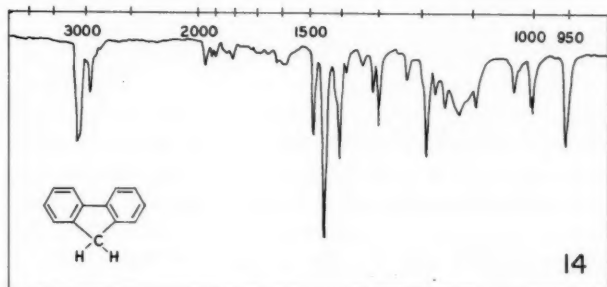
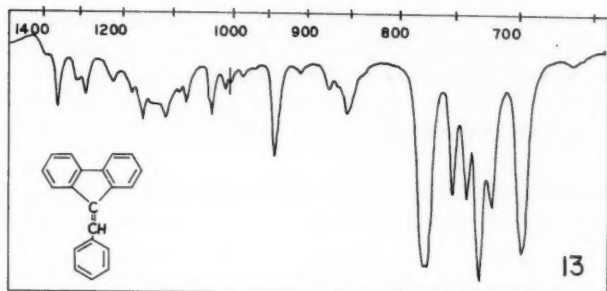
The monomethyl-, monobenzyl- and monoallyl-fluorene (Figs. 4, 5, 8, 11) all show very strong reduction of intensity or complete elimination of absorption at 952  $\text{cm}^{-1}$ , any residual absorption again being due to contamination by unreacted fluorene.

As expected, 9-benzylidene-fluorene shows no absorption in the 950–956  $\text{cm}^{-1}$  region



FIGS. 9-12.

(Fig. 13). A similar result occurs for the other 9,9-disubstituted fluorenes (Figs. 7, 9, 12). The position of the absorption for the remaining C<sub>9</sub>-H bond in the monosubstituted fluorenes is determined by deuteration. Comparison of Figs. 5 and 6 show that two bands,



FIGS. 13-15.

792  $\text{cm}^{-1}$  and 722  $\text{cm}^{-1}$ , are eliminated on deuteration, hence it is clear that these are due to  $\text{C}_9\text{—H}$  in 9-monomethylfluorene. Whether one of these corresponds to the absorption of the methylene group at 952  $\text{cm}^{-1}$  is not known. Similarly, the bands at 787  $\text{cm}^{-1}$  (weak) and 719  $\text{cm}^{-1}$  (strong) in the spectrum of 9-monobenzylfluorene (Figs. 8 and 10) and those at 789  $\text{cm}^{-1}$  (weak) and 727  $\text{cm}^{-1}$  (strong) in the 9-monoallylfluorene (Fig. 11) are likewise to be associated with the remaining  $\text{C}_9\text{—H}$  bond, since deuteration or disubstitution eliminates the absorption.

In addition it might be pointed out that the bands at 1100, 1167, and 1185  $\text{cm}^{-1}$  are eliminated upon deuteration of the 9-monomethylfluorene (Figs. 5 and 6) hence can be considered as associated with the remaining  $\text{C}_9\text{—H}$  bond.

#### *The 1190 $\text{cm}^{-1}$ Band*

The cause of absorption at this frequency is not known. It was at first believed to be composed of absorption due to the methylene group *and* to some other structural feature



since monodeuteration reduces it to about one-half its former intensity while dideuteration produces little further change (Figs. 1-3). However, monosubstitution reduces the band markedly while disubstitution practically removes it, hence the absorption seen at  $1190\text{ cm}^{-1}$  in the dideuterated molecule may be due to shifts, or combinations of overtones, stemming from deuteration at  $C_9$ .

The frequency of the  $\begin{array}{c} | \\ -C-D \\ | \end{array}$  bond is thought to appear at  $827\text{ cm}^{-1}$  in agreement with the calculated value.

The position of absorption of the remaining  $\begin{array}{c} | \\ -C-H \\ | \end{array}$  bond as affected by the presence of the deuterium atom could not be defined in view of the complexity of the neighboring bands.

#### *The $1298\text{ cm}^{-1}$ Band*

This absorption is probably due to methylene wagging vibration (16) and, in agreement with previous observations, is of lower intensity than that from rocking vibration. The band is reduced on monodeuteration or monosubstitution at  $C_9$  while dideuteration or disubstitution largely eliminates it. Neighboring absorption bands mask these effects somewhat with the result that this frequency is less useful than are the others mentioned above.

The  $\begin{array}{c} | \\ -C-D \\ | \end{array}$  bond frequency appears at  $939\text{ cm}^{-1}$  in the monodeuterated molecule. Since its intensity is practically unchanged upon dideuteration, the view is supported that it is a composite band in the monodeuterated structure, with a contribution from the remaining  $\begin{array}{c} | \\ -C-H \\ | \end{array}$  band shifted slightly from  $952\text{ cm}^{-1}$ . Dideuteration removes this contribution but adds that from the second C—D bond in dideuterated fluorene ( $1298\text{ cm}^{-1}$  shifted to  $939\text{ cm}^{-1}$ ).

#### *The $1400\text{ cm}^{-1}$ Band*

This absorption is quite likely derived from scissoring vibration of the methylene group (16) since any type of mono- or di-substitution at  $C_9$  eliminates this band. The absorption attributed to the new  $\begin{array}{c} | \\ -C-D \\ | \end{array}$  bond obtained on monodeuteration might be that appearing at  $974\text{ cm}^{-1}$  and increasing on dideuteration. This agrees quite well with the calculated value (Table I). The band at  $1038\text{ cm}^{-1}$  appearing on monodeuteration and increasing in magnitude upon dideuteration agrees roughly with the calculated shift, but examination of the spectra of mono- and di-substituted compounds (Figs. 1-13) shows that *any mono- or di-substitution* at  $C_9$  gives rise to a band, increasing upon disubstitution, at about the same frequency. Hence the absorption at  $1038\text{ cm}^{-1}$  certainly cannot be due to the  $\begin{array}{c} | \\ -C-D \\ | \end{array}$  bond.

#### *The $2930\text{ cm}^{-1}$ Band*

This absorption, arising from C—H stretching frequency, must be due to the methylene

group since it disappears upon deuteration (Figs. 14 and 15).<sup>\*</sup> No firm assignment could be made for the  $\text{—}\overset{\textstyle |}{\text{C}}\text{—D}$  band, although weak absorption appears at  $2150\text{ cm}^{-1}$  in the deuterated molecule (Table I) in agreement with the calculated shift.

#### USEFUL BANDS ASSOCIATED WITH PARTICULAR SUBSTITUENTS AT C<sub>9</sub>

In all the spectra there is clearly discernible a characteristic strong band at  $738\text{ cm}^{-1}$  originating from the two ortho disubstituted benzene nuclei in fluorene (16). Monomethyl-, monoallyl-, and monobenzyl-fluorene and 9-benzylidene fluorene all show weak absorption between  $787$  and  $793\text{ cm}^{-1}$  and strong absorption in the region of  $719$  to  $728\text{ cm}^{-1}$  (overlapping to some extent with the major  $738\text{ cm}^{-1}$  band). Only for monomethylfluorene is this latter absorption of weaker intensity, though still quite readily discernible, and the former stronger than in all the other cases examined. Disubstitution at C<sub>9</sub> removed this absorption completely. We have attributed these two bands to the remaining C<sub>9</sub>—H bond. The  $719$ – $728\text{ cm}^{-1}$  band has been used to differentiate between the mono- and di-substitution and, in particular, to follow the preparation, purification, and identification of 9-monoallylfluorene and 9,9-diallylfluorene whose mixtures with each other and with fluorene itself are separated with difficulty.

Clear distinction of the methylated fluorenes from the allyl or benzyl fluorenes may be made by observation of the strong, isolated band at  $758\text{ cm}^{-1}$  in the spectrum of monomethylfluorene, which doubles in intensity upon dimethylation. The monomethyl compound shows another medium-weak, though impressive, band at  $793\text{ cm}^{-1}$  which is eliminated upon dimethylation or on deuteration of the remaining C<sub>9</sub>—H. Allylfluorenes absorb at  $913\text{ cm}^{-1}$ , the intensity of the diallyl being approximately double that found for the monoderivative. This absorption is no doubt that associated with the C—H out-of-plane bending found in olefinic structures (16). The band appearing at  $681\text{ cm}^{-1}$  for mono- and di-allylfluorene may also be of analytical value.

The strong absorption at  $700\text{ cm}^{-1}$  in 9-monobenzylfluorene (approximately doubled in the dibenzylfluorene) is due to the monosubstituted benzene moiety. Also of some assistance in identifying 9-benzylated fluorenes is the weak band at  $905$  to  $909\text{ cm}^{-1}$ . This appears to be present in 9-benzylidene fluorene. Whether the same absorption is to be found in the allyl fluorenes cannot be shown since the strong  $913\text{ cm}^{-1}$  band interferes.

Of some assistance is the strong absorption at  $761$  to  $764\text{ cm}^{-1}$  for diallyl- and dibenzylfluorene, whereas for the monoallyl- and monobenzyl-fluorenes a similar strong absorption occurs at  $754\text{ cm}^{-1}$ . Furthermore, a band at  $746$  to  $748\text{ cm}^{-1}$  appears for the mono- and di-benzylfluorene but not for mono- and di-allylfluorene.

The view that the dipotassium compound had been made from two equivalents of potassium and one of fluorene is supported by deuteration experiments. The 9-fluorenyl-potassium (also the 9-fluorenylsodium, prepared by Greenhow's method (3)), treated with excess deuterium oxide gave a spectrum (Fig. 2) in which the shifted frequency, due to C<sub>9</sub>—H, is thought to be at  $677\text{ cm}^{-1}$ . If this assignment is correct, dideuteration should eliminate this band. Such elimination is actually observed in the spectrum of the dideuterated compound obtained from the experiment wherein two equivalents of potassium to one of fluorene were used. No change in extent of deuteration was found when a greater proportion of potassium metal was employed.

<sup>\*</sup>The spectra for Figs. 14 and 15 were obtained in CCl<sub>4</sub> solution.

## EXPERIMENTAL

The fluorene used in this work was Eastman Kodak 98% practical grade.

Infrared spectra were obtained with the aid of a Perkin-Elmer model 21 double-beam spectrophotometer equipped with a sodium chloride prism. Solutions in carbon tetrachloride and carbon disulphide, containing 20 mg solute per ml of solvent were measured in sodium chloride cells of 0.5-mm thickness.

All melting points are uncorrected.

*9-Fluorenylpotassium*

Fluorene (8.3 g, 0.05 mole) and potassium metal (1.95 g, 0.05 mole) were heated in refluxing purified dioxane (19) protected by an atmosphere of purified dry nitrogen. In 3 hours all the potassium was consumed. The reaction mixture was cooled to room temperature and the reddish-brown precipitate isolated by filtration under suction and washed with dry hexane to remove unreacted fluorene. Isolation of the monopotassium compound was best carried out in a dry box containing an atmosphere of nitrogen. Samples for analysis were prepared by freeing the fluorenyl potassium from adhering solvent with a stream of nitrogen drawn through the solid product by suction. Analysis was carried out by first treating a weighed portion of the solid with water then titrating the basic solution with standard acid. In three attempts at analyses the "purified" precipitate showed values of 14.9, 15.3, and 15.7% for potassium. The value required for  $C_{13}H_9K$  is 19.15%.

*9-Deuteriofluorene*

The 9-fluorenylpotassium was prepared from 1.66 g of fluorene and 0.39 g of potassium in 5 ml of pure dioxane refluxed for 3 hours until all the potassium had reacted. One milliliter of  $D_2O^*$  (95%) was slowly added and the mixture then stirred for 1 hour. Following the addition of ether, the dioxane and potassium hydroxide were readily removed by extracting the solution of deuterated fluorene with water. When the ethereal solution was dried and the solvent removed there was obtained, upon crystallization of the resulting solid from alcohol, 1.58 g of monodeuterated fluorene.

Analysis for deuterium by N.M.R. show approximately 75% monodeuteration.

*9,9-Dideuteriofluorene*

A mixture of 0.01 mole (1.66 g) of fluorene and 0.02 mole (0.78 g) of potassium was heated for 3.5 hours in 5 ml of refluxing dioxane till all the potassium had been consumed. The addition of 1.5 ml of  $D_2O$  and isolation of the product as before gave 1.56 g of dideuterated fluorene.

N.M.R. analysis shows complete absence of absorption at the position attributable to  $>CH_2$ , indicating complete dideuteration.

*9-Methylfluorene*

This compound was prepared by the following modification of Greenhow's procedure (3). Fluorene (18 g) and finely powdered sodamide (3.9 g) were heated in a nitrogen atmosphere for 5 hours at 180° C in 50 ml of decahydronaphthalene (dried with sodium and distilled). When the reaction mixture had cooled to room temperature, the solvent was decanted and the remaining black amorphous solid which adhered to the lower portion of the flask was washed several times with hexane (dried with sodium). Methyl iodide (12 ml) in 50 ml of hexane was then added and the magnetically stirred mixture refluxed for 12 hours under nitrogen. After the cautious addition of water to dissolve the

\*The  $D_2O$  was donated by the National Research Council of Canada.

potassium iodide, the hexane layer was separated, dried, and the solvent removed. The yellow oil obtained, dissolved in pentane and cooled in a refrigerator, deposited unchanged fluorene. Further purification was accomplished by chromatography of the pentane mother liquor on a 50-cm column of dry, activated alumina (80–200 mesh). The first fraction, obtained by elution with hexane, gave 9-methylfluorene, m.p. 43–44° C. Further purification by repeated chromatography altered the infrared spectrum slightly and changed the melting point of the compound to 45–46° C, lit. 45–47° C (3). (Compare the melting point of 58° reported by Wieland (17).)

#### *9,9-Dimethylfluorene*

A solution of 16.6 g of fluorene in 80 ml of dioxane containing 7.8 g of potassium was boiled for 5 hours under an atmosphere of nitrogen. All the potassium was consumed in this time. The slow addition of 20 ml of methyl iodide, to the cooled mixture, produced a vigorous but controllable reaction. Stirring was continued for 1 hour whereupon both ether and water were added to the reaction flask. Several extractions of the ethereal solution with water removed the dioxane. The dried ( $\text{CaCl}_2$ ) solution was freed from ether and gave a yellow oil which could not be purified adequately by fractional distillation. However, chromatography with alumina of an hexane solution of this oil separated the unchanged fluorene and monomethyl compound from dimethylfluorene. The first fraction gave the 9,9-dimethylfluorene, m.p. 88–89° C, but when crystallized from methanol melted at 95–96° C, lit. 95–96° C (20). It is interesting that recrystallization from pentane of the 95–96° C melting compound gave a lower and less definite melting point, found in one case to be 78–83° C, which after a second crystallization from pentane gave 81–87° C.

#### *9-Benzylfluorene*

The 9-fluorenylsodium was prepared from 18.3 g of fluorene and 3.9 g of sodamide heated in decahydronaphthalene for 4 hours at 180° C under a nitrogen atmosphere (3). The black solid, deposited in the flask, was washed with hexane as in the preparation of 9-methylfluorene and treated with a solution of 40 ml of benzyl chloride in 40 ml of hexane. This mixture was refluxed for 20 hours. To the hexane solution, now diluted with ether, was added water to remove the sodium chloride. Removal of the ether hexane solvent gave a yellow amorphous product which after solution in alcohol deposited 12.5 g of crystalline 9-benzylfluorene melting sharply at 134° C, lit. 135° C (3). Further purification by chromatography on activated alumina raised the melting point to 136° C. Crystallization from alcohol did not change the melting point.

#### *9,9-Dibenzylfluorene*

(a) *From fluorene.*—To the dioxane containing 9,9-fluorenyldipotassium (made from 16.6 g of fluorene and 7.8 g of potassium in 80 ml of dioxane) was added 21 ml of benzyl chloride (an excess). The product of this reaction, only slightly soluble in ether, was isolated quite simply by the addition of water and ether to the dioxane solution whereupon the solid which formed could then be removed by filtration. The 9,9-dibenzylfluorene weighed 11.2 g and melted at 146° C (from alcohol), lit. 147–148° C (13).

(b) *From 9-benzylfluorene.*—A mixture of 2.6 g of 9-benzylfluorene and 0.39 g of potassium metal (equimolar portions) in 12 ml of dioxane was heated till solution of the metal was complete. Forty minutes of refluxing with 1.2 ml of benzyl chloride gave a solid, isolated as above, with properties and melting point identical with those of 9,9-dibenzylfluorene.

*9-Deutero-9-benzylfluorene*

Dioxane (15 ml) containing 2.56 g of *9-benzylfluorene* and 0.39 g of potassium was boiled for 40 minutes, cooled to room temperature, and treated with 0.8 ml (excess) of  $D_2O$ . The red precipitate disappeared and the product, isolated as usual by employing ether and water, and crystallized from alcohol, melted at  $131^\circ C$ , yield 0.5 g. Chromatography raised the melting point to  $134^\circ C$ , which crystallization from alcohol did not change.

*9-Deutero-9-methylfluorene*

This compound was prepared in the same manner as for *9-deutero-9-benzylfluorene* and isolated as was *9-methylfluorene*, m.p.  $45.5^\circ C$ .

*9-Benzylidenefluorene*

The procedure was a modified version of that employed by Thiele and Henle (13). The use of potassium ethylate, rather than sodium ethylate, gave the product in 3 days as compared with 14 days reported for Thiele and Henle's method.

To a solution of 2.5 g of potassium in 125 ml of dry ethyl alcohol was added 5 g of fluorene. Freshly distilled benzaldehyde (4.5 g) in 10 ml of alcohol was added and the reaction mixture kept at  $45^\circ C$  for 3 days. The *9-benzylidenefluorene* (3.6 g) deposited from the solution was crystallized once from alcohol, m.p.  $74^\circ-75^\circ C$ , lit.  $76^\circ C$  (13).

*9-Allylfluorene*

This compound was prepared by a modification of Greenhow's method (3).

Sodamide (3.9 g) and fluorene (18 g) were heated in refluxing decalin (40 ml) for 4 hours (nitrogen atmosphere). The decalin was then replaced by pentane (50 ml) and the *9-fluorenylsodium* treated with 50 ml of allyl bromide (excess). After 8 hours reflux the product was isolated by removing the sodium chloride with water, then eliminating the solvent as well as the excess allyl bromide. Vacuum distillation gave 11.5 g of a light-yellow liquid boiling at  $132-137^\circ C/3$  mm. Elution chromatography as described for the methylated fluorenes gave a sample suitable for infrared analysis.

*9,9-Diallylfluorene*

Fluorene (8.3 g) and potassium metal (3.9 g) were boiled for 4 hours in 100 ml of dioxane ( $N_2$ ). When the reaction mixture was cooled to room temperature and treated with 8.65 ml of allyl bromide, added dropwise, an exothermic reaction occurred with simultaneous disappearance of the reddish-brown precipitate. After an additional period of stirring for 5 hours the product was isolated as usual by the addition of ether and water. The crude oil (12.1 g) obtained from the ether layer was fractionally distilled under vacuum to yield 7.9 g of light-yellow oil, b.p.  $144^\circ C/3$  mm, which was submitted to chromatography for additional purification.

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## THE PREPARATION OF SOME THIOSEMICARBAZONES AND THEIR COPPER COMPLEXES. PART I<sup>1</sup>

B. A. GINGRAS, R. W. HORNAL, AND C. H. BAYLEY

### ABSTRACT

A number of thiosemicarbazones and their 1:1 copper complexes are described and the possible structures of the latter are discussed. Formation of copper complexes from aromatic aldehyde and ketone thiosemicarbazones results in a loss of one H atom as indicated by infrared spectra. In the aliphatic series, no loss of H atom is apparent upon complex formation. It is reasonable to assume that different processes are involved resulting in two possible structures for the aromatic and the aliphatic copper complexes. Some chemical evidence supports this view.

Since the discovery by Domagk (1) of the antitubercular activity of thiosemicarbazones, a number of papers on the pharmacology of this type of compounds have been published (2, 3, 4, 5). Thiosemicarbazones have also been found active in preventing the growth of certain fungi (6, 7). It has been assumed that the microbial activity of thiosemicarbazones is due to their ability to chelate traces of metal (e.g. copper), the metal complexes themselves being the active ingredients (8).

This hypothesis has been substantiated somewhat by the fact that selenosemicarbazones, in which the sulphur atom is replaced by selenium, are more active against fungi than the corresponding thiosemicarbazones, which in turn are more active than semicarbazones. This difference in activity is attributed to the formation of metal complexes which would occur more readily in the case of selenosemicarbazones (9).

There is considerable experimental evidence to support the view that formation of a toxic metal-organometal complex is a possible mechanism of fungicidal action. Albert *et al.* (10) have shown that 8-hydroxyquinoline is relatively non-toxic in triple-distilled water, but that addition of a trace of an iron salt makes it effective. Similarly, Cymerman-Craig *et al.* (11) showed quite conclusively that the high specific activity of isonicotinic hydrazide against *Mycobacterium tuberculosis* is due to formation of a metal complex. The high fungistatic activity of the dithiocarbamates is also believed to be due to their ability to bind metals (12, 13). It is also of interest to note that activity is lost completely when the terminal  $\text{—NH}_2$  group of *p*-acetamidobenzaldehyde thiosemicarbazone is replaced by  $\text{—SCH}_3$ , the most likely explanation being that the latter group would prevent chelation (14).

In a search for new fungicides and also to test further the hypothesis discussed above, a number of thiosemicarbazones (II) of aliphatic and aromatic aldehydes and ketones and their copper complexes have been prepared, and their activity against two fungi have been examined.

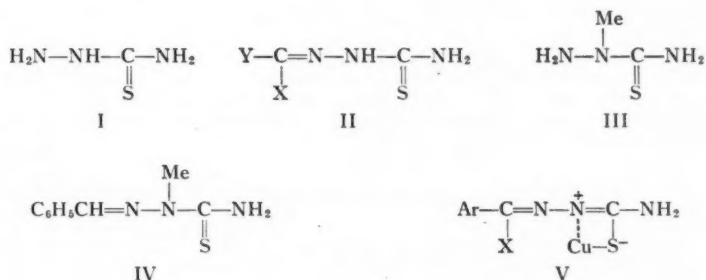
Previous workers have described copper complexes of *p*-substituted benzaldehyde thiosemicarbazones (namely *p*-methoxy- and *p*-acetamido-) and their use in chemotherapy of tuberculosis has been discussed briefly (15). Metallic complexes of a few thiosemicarbazones have also been obtained and their properties discussed mostly in connection with methods of quantitative analysis for cations; the fungicidal activity of the mercury complexes of these compounds has been investigated and they have been found to be inactive (16).

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No systematic investigation of the thiosemicarbazones and the possibility of their chelation with metals in relation to their microbiological activity seems to have been made. The purpose of the work described in this paper was to prepare a series of thiosemicarbazones and their copper complexes for use in subsequent studies of their fungicidal properties.

Most of the thiosemicarbazones listed in Table I gave copper complexes. A number of thiosemicarbazones and all of the copper complexes shown are described for the first time. The latter are colored solids of very low solubility in water and organic solvents. The least soluble were the aliphatic ones and consequently, their purification has been particularly tedious and in the case of the  $C_3$ ,  $C_4$ , and  $C_5$  compounds the elementary analysis remains unsatisfactory. However, since they show the expected infrared spectra and copper contents which are in good agreement with the theoretical values, they have been included in the data presented. Some others, viz. acetophenone and *p*-bromoacetophenone, decomposed during the various purification treatments used. The copper complexes are listed in Table II. Most of them underwent no change in color as the result of exposure to daylight and artificial light in the laboratory. In only two, i.e. furfural and *m*-nitrobenzaldehyde, was there any evidence of decomposition.



On the basis of elementary analysis, there can be no doubt that copper and thiosemicarbazones react in a 1:1 ratio. In the aromatic series the infrared spectra of the copper complexes show only two bands in the  $-\text{NH}-$  stretching region (at about  $3450\text{ cm}^{-1}$  and  $3350\text{ cm}^{-1}$ , see Table II) whilst the grouping  $-\text{NH}-\text{CS}-\text{NH}_2$  accounts for three bands (at about  $3440$ ,  $3240$ , and  $3150\text{ cm}^{-1}$ , see Table I) in the case of the free thiosemicarbazones. This indicates that one hydrogen atom is involved in the complex formation.

By a study of the infrared spectra alone, it is difficult to discriminate between those three bands as any of the H atoms in II may take part in bonding, with a resulting shift to lower frequencies (17).

However, in the case of benzaldehyde, when the H atom of the  $-\text{NH}-$  group in II ( $\text{Y} = \text{C}_6\text{H}_5$ ,  $\text{X} = \text{H}$ ) was replaced by a methyl group, the resulting benzaldehyde methylthiosemicarbazone (IV) did not form a copper complex. Although more experimental evidence is required, this suggests that the H atom of the secondary  $-\text{NH}-$  group is responsible for the complex formation. A logical structure for the aromatic copper complexes would thus be as in V. It is now possible to speculate that the vibrations of the terminal  $-\text{NH}_2$  group are responsible for the two bands at higher frequencies, since these are also present in the spectra of the copper complexes at about the same

TABLE I  
Thiosemicarbazones: 
$$\begin{array}{c} \text{Y}-\text{C}=\text{N}-\text{NH}-\text{C}-\text{NH}_2 \\ | \qquad \qquad \qquad || \\ \text{X} \qquad \qquad \qquad \text{S} \end{array}$$

Y	X	M.p., °C	Lit. m.p., °C	Yield, %	Solvents used in recrystallization	Typical I.R. absorption in the —NH— region, cm <sup>-1</sup>	Formula	Found, %	Calculated, %
CH <sub>3</sub>	CH <sub>3</sub>	181	179 <sup>c</sup>	75	EtOH-H <sub>2</sub> O	3380-3240-3150	C <sub>6</sub> H <sub>9</sub> N <sub>3</sub> S		
C <sub>2</sub> H <sub>5</sub>	H	162	159 <sup>c</sup>	55	EtOH-H <sub>2</sub> O	3380-3270-3150	C <sub>8</sub> H <sub>9</sub> N <sub>3</sub> S		
<i>n</i> -C <sub>3</sub> H <sub>7</sub>	H	108	108-109 <sup>f</sup>	67	EtOH-H <sub>2</sub> O	3380-3250-3140	C <sub>9</sub> H <sub>11</sub> N <sub>3</sub> S		
<i>n</i> -C <sub>4</sub> H <sub>9</sub>	H	64	65 <sup>d</sup>	40	Benzene - <i>n</i> - hexane	3400-3260-3160	C <sub>10</sub> H <sub>13</sub> N <sub>3</sub> S		
iso-C <sub>4</sub> H <sub>9</sub>	H	58	52-53 <sup>d</sup>	75	EtOH-H <sub>2</sub> O	3400-3260-3150	C <sub>10</sub> H <sub>13</sub> N <sub>3</sub> S	C, 51.24	C, 51.33
<i>n</i> -C <sub>6</sub> H <sub>13</sub>	H	68		65	EtOH-H <sub>2</sub> O	3400-3250-3150	C <sub>12</sub> H <sub>17</sub> N <sub>3</sub> S	H, 9.16	H, 9.09
								N, 22.58	N, 22.45
								S, 17.54	S, 17.12
<i>n</i> -C <sub>7</sub> H <sub>15</sub>	H	96	94-95 <sup>h</sup>	94	EtOH-H <sub>2</sub> O	3390-3260-3150	C <sub>13</sub> H <sub>19</sub> N <sub>3</sub> S		
<i>n</i> -C <sub>8</sub> H <sub>17</sub>	H	77	77 <sup>h</sup>	82	EtOH-H <sub>2</sub> O	3420-3260-3160	C <sub>14</sub> H <sub>21</sub> N <sub>3</sub> S		
<i>n</i> -C <sub>9</sub> H <sub>19</sub>	H	102	100 <sup>h</sup>	80	EtOH	3400-3260-3160	C <sub>15</sub> H <sub>23</sub> N <sub>3</sub> S	C, 59.68	C, 59.2
<i>n</i> -C <sub>10</sub> H <sub>21</sub>	H	86		93	EtOH	3405-3260-3160	C <sub>16</sub> H <sub>25</sub> N <sub>3</sub> S	H, 10.08	H, 10.28
								N, 17.05	N, 17.28
								S, 12.90	S, 13.18
<i>o</i> -C <sub>10</sub> H <sub>19</sub>	H	72		81	<i>n</i> -Hexane	3400-3270-3160	C <sub>15</sub> H <sub>23</sub> N <sub>3</sub> S	C, 59.89	C, 59.7
								H, 9.55	H, 9.55
								N, 17.30	N, 17.41
								S, 13.30	S, 13.28
<i>n</i> -C <sub>11</sub> H <sub>23</sub>	H	105	100 <sup>h</sup>	88	EtOH	3400-3280-3170	C <sub>16</sub> H <sub>27</sub> N <sub>3</sub> S	C, 62.54	C, 62.00
<i>n</i> -C <sub>11</sub> H <sub>23</sub>	CH <sub>3</sub>	99		96	EtOH	3400-3240-3140	C <sub>16</sub> H <sub>25</sub> N <sub>3</sub> S	H, 10.58	H, 10.69
								N, 15.60	N, 15.49
								S, 11.80	S, 11.80
<i>n</i> -C <sub>13</sub> H <sub>27</sub>	CH <sub>3</sub>	103		90	EtOH	3400-3240-3140	C <sub>18</sub> H <sub>27</sub> N <sub>3</sub> S	C, 65.95	C, 66.2
								H, 11.32	H, 11.3
								N, 12.98	N, 12.85
								S, 9.65	S, 9.8
CH <sub>3</sub>	CO <sub>2</sub> H	201		57	EtOH-H <sub>2</sub> O	3430-3310-3200	C <sub>11</sub> H <sub>7</sub> N <sub>3</sub> O <sub>2</sub> S	C, 29.78	C, 29.82
								H, 4.70	H, 4.35
								N, 25.80	N, 26.08
								S, 19.80	S, 19.88
H <sub>2</sub> N—CS—NH—N=	H	>300	>300 <sup>g</sup>	85	Washed with	3405-3270-3160	C <sub>6</sub> H <sub>5</sub> N <sub>3</sub> S <sub>2</sub>		
CH—					EtOH-acetone				
CH <sub>2</sub> —CH <sub>2</sub> —CH <sub>2</sub> —		166	165-167 <sup>a</sup>	97	EtOH	3370-3200-3130	C <sub>7</sub> H <sub>13</sub> N <sub>3</sub> S		
CH <sub>2</sub> —CH <sub>2</sub> —									
HC=CH—CH=C—	H	160	182-183 <sup>a</sup>	85	EtOH	3400-3210-3120	C <sub>6</sub> H <sub>7</sub> N <sub>3</sub> OS		
			148 <sup>b</sup>						
C <sub>6</sub> H <sub>5</sub>	H	162	160 <sup>a</sup>	81	EtOH	3420-3240-3140	C <sub>12</sub> H <sub>9</sub> N <sub>3</sub> S		
<i>o</i> -OHC <sub>6</sub> H <sub>4</sub>	H	230	235 <sup>a</sup>	100	EtOH-acetone	3440-3330-3180	C <sub>13</sub> H <sub>9</sub> N <sub>3</sub> OS		
			231 <sup>c</sup>						
<i>m</i> -OHC <sub>6</sub> H <sub>4</sub>	H	167	137 <sup>a</sup>	50	Acetone-ether	3430-3280-3150	C <sub>13</sub> H <sub>9</sub> N <sub>3</sub> OS		
			174 <sup>b</sup>						
<i>p</i> -OHC <sub>6</sub> H <sub>4</sub>	H	228	236 <sup>a</sup>	50	EtOH	3460-3410-3310	C <sub>13</sub> H <sub>9</sub> N <sub>3</sub> OS		
			224 <sup>c</sup>						
<i>m</i> -O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub>	H	229	239-40 <sup>a</sup>	78	Acetone	3380-3220-3120	C <sub>13</sub> H <sub>9</sub> N <sub>3</sub> O <sub>2</sub> S		
			163 <sup>c</sup>						
<i>o</i> -FC <sub>6</sub> H <sub>4</sub>	H	185		81	EtOH-H <sub>2</sub> O	3420-3240-3140	C <sub>12</sub> H <sub>7</sub> FN <sub>3</sub> S	C, 48.83	C, 48.73
								H, 4.37	H, 4.06
								N, 21.50	N, 21.32
								S, 16.35	S, 16.24
<i>m</i> -FC <sub>6</sub> H <sub>4</sub>	H	192		73	EtOH	3400-3240-3160	C <sub>12</sub> H <sub>7</sub> FN <sub>3</sub> S	C, 48.54	C, 48.73
								H, 4.39	H, 4.06
								N, 21.20	N, 21.32
								S, 16.40	S, 16.24

TABLE I (Concluded)

$$\text{Y}-\text{C}=\text{N}-\text{NH}-\text{C}-\text{NH}_2$$

$$\quad \quad \quad \text{X} \quad \quad \quad \text{S}$$

Thiosemicarbazones:

Y	X	M.p., °C	Lit. m.p., °C	Yield, %	Solvents used in recrystallization	Typical I.R. absorption in the —NH— region, cm <sup>-1</sup>	Formula	Found, %	Calculated, %
<i>p</i> -FC <sub>6</sub> H <sub>4</sub>	H	193	180 <sup>d</sup>	42	EtOH-H <sub>2</sub> O	3390-3230-3140	C <sub>6</sub> H <sub>4</sub> FN <sub>2</sub> S	N, 21.40 S, 16.25	N, 21.32 S, 16.24
<i>o</i> -ClC <sub>6</sub> H <sub>4</sub>	H	221	223 <sup>a</sup>	97	EtOH	3420-3250-3150	C <sub>6</sub> H <sub>3</sub> ClN <sub>2</sub> S		
<i>p</i> -ClC <sub>6</sub> H <sub>4</sub>	H	219	220 <sup>a</sup>	95	EtOH	3420-3280-3150	C <sub>6</sub> H <sub>3</sub> ClN <sub>2</sub> S		
2,5-F(NO <sub>2</sub> )C <sub>6</sub> H <sub>3</sub>	H	245		63	Acetone-MeOH -hexane	3400-3240-3140	C <sub>6</sub> H <sub>2</sub> N <sub>2</sub> O <sub>2</sub> S	N, 24.40 S, 14.05	N, 25.1 S, 14.35
<i>p</i> -(OCH <sub>3</sub> )C <sub>6</sub> H <sub>4</sub>	H	178	178 <sup>a</sup>	81	EtOH	3420-3305-3150	C <sub>6</sub> H <sub>11</sub> N <sub>2</sub> OS		
2,5-OH(Cl)C <sub>6</sub> H <sub>3</sub>	H	287-290	281-282 <sup>a</sup>	72	EtOH-H <sub>2</sub> O	3420-3240-3160	C <sub>6</sub> H <sub>3</sub> ClN <sub>2</sub> OS		
2,4-(Cl) <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	H	238	245 <sup>a</sup>	83	EtOH	3440-3250-3140	C <sub>6</sub> H <sub>2</sub> Cl <sub>2</sub> N <sub>2</sub> S		
2,4(OH) <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	H	236	239-240 <sup>a</sup>	76	EtOH	3480-3350-3160	C <sub>6</sub> H <sub>3</sub> N <sub>2</sub> O <sub>2</sub> S		
C <sub>6</sub> H <sub>5</sub>	CH <sub>3</sub>	122	118-119 <sup>a</sup>	96	EtOH-H <sub>2</sub> O	3410-3220-3140	C <sub>7</sub> H <sub>11</sub> N <sub>2</sub> S		
<i>m</i> -H <sub>2</sub> NC <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub>	148	152-154 <sup>a</sup>	37	EtOH	3410-3210-3140	C <sub>7</sub> H <sub>12</sub> N <sub>2</sub> S		
<i>p</i> -ClC <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub>	202	205-206 <sup>a</sup>	96	EtOH	3420-3200-3140	C <sub>7</sub> H <sub>10</sub> ClN <sub>2</sub> S		
<i>p</i> -BrC <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub>	204	203 <sup>a</sup>	98	EtOH-H <sub>2</sub> O	3410-3200-3130	C <sub>7</sub> H <sub>10</sub> BrN <sub>2</sub> S		
C <sub>6</sub> H <sub>5</sub> CH(OH)	C <sub>6</sub> H <sub>5</sub>	179	176-178 <sup>a</sup>	80	EtOH-H <sub>2</sub> O	3420-3240-3150	C <sub>13</sub> H <sub>15</sub> N <sub>2</sub> OS		
C <sub>6</sub> H <sub>5</sub> CO	C <sub>6</sub> H <sub>5</sub>	96	96 <sup>a</sup>	91	EtOH-H <sub>2</sub> O	Not well defined	C <sub>13</sub> H <sub>13</sub> N <sub>2</sub> OS		
C <sub>6</sub> H <sub>5</sub> NHCOCH <sub>3</sub>	CH <sub>3</sub>	158		87	EtOH	3430-3250-3120	C <sub>11</sub> H <sub>14</sub> N <sub>2</sub> OS	C, 52.26 H, 6.06 N, 22.30 S, 12.76	C, 52.8 H, 5.6 N, 22.4 S, 12.8

<sup>a</sup>P. P. T. Sah and T. C. Daniels. *Rec. trav. chim.* **69**, 1545 (1950).

<sup>b</sup>D. Libermann, M. Moyeux, A. Rouaix, J. Maillard, L. Hengl, and J. Himbert. *Bull. soc. chim.* 957 (1953).

<sup>c</sup>F. Wild. *Characterization of organic compounds*. 2nd ed. Cambridge University Press, 1958, pp. 139-141.

<sup>d</sup>Ng. Ph. Buu-Hoi, Ng. D. Xuong, and F. Binon. *J. Chem. Soc.* 713 (1956).

<sup>e</sup>B. Holmberg. *Arkiv Kemi.* **9**, 65-80 (1955).

<sup>f</sup>L. K. Evans and A. E. Gillam. *J. Chem. Soc.* 565 (1943).

<sup>g</sup>C. Neuberg and W. Neimann. *Ber.* **2**, 2049 (1902).

<sup>h</sup>A. H. Uhl. *J. Am. Pharm. Assoc.* **24**, 381 (1935).

<sup>i</sup>G. N. Mitra and S. S. Guha-Sircar. *J. Indian Chem. Soc.* **32** (7), 435 (1955).

frequencies, or, at the most, with only a slight shift to the left. In the thiosemicarbazones the secondary —NH— group would be responsible for the lower frequency band at about 3150 cm<sup>-1</sup>.

There is no doubt that the nature of Y and X in formula II has a definite effect on the availability of the H atom of the secondary —NH— group to take part in complex formation. When Y is aromatic, both the inductive (—I) and mesomeric effects may alter the electronic density at the nitrogen atom resulting in the weakening of the —N—H bond. When Y is aliphatic, the inductive effect (+I) would affect the —N—H bond in a reverse manner and it is likely that the formation of a copper complex proceeds by another route. Infrared spectra in these cases show consistently three bands in the —NH— stretching region for both free thiosemicarbazones and their copper complexes. On this basis pyruvic acid thiosemicarbazone-copper would be expected to behave like the aromatic compounds, because of the (—I) inductive effect of the carboxyl group. This is indeed the case, as the infrared spectrum of this complex shows two bands, instead of three, in the —NH— region. Similarly, the infrared spectrum of cyclohexanone thiosemicarbazone-copper is similar to that of the aliphatic compounds, whereas furfural thiosemicarbazone-copper gives a spectrum typical of an aromatic compound in the —NH— stretching region.

TABLE II

Thiosemicarbazone-copper complexes:  $\left( \begin{array}{c} \text{Y}-\text{C}=\text{N}-\text{NH}-\text{C}-\text{NH}_2 \\ | \quad \quad \quad || \\ \text{X} \quad \quad \quad \text{S} \end{array} \right) \text{Cu}$ 

Y	X	M.p., °C	Yield	Methods of purifica- tion	Typical I.R. absorptions in the —NH— region, cm <sup>-1</sup>	Formula	Found, %	Calculated, %
CH <sub>3</sub>	CH <sub>3</sub>	174	91	<i>f, d</i>	3450-3290-3150	C <sub>4</sub> H <sub>8</sub> N <sub>2</sub> SCu	C, 24.66 H, 4.01 N, 21.80 S, 16.95	C, 24.8 H, 4.13 N, 21.65 S, 16.52
C <sub>2</sub> H <sub>5</sub>	H	128	67	<i>a, b, d, e</i>	3420-3270-3150	C <sub>6</sub> H <sub>10</sub> N <sub>2</sub> SCu	Cu, 32.8	Cu, 32.8
<i>n</i> -C <sub>3</sub> H <sub>7</sub>	H	168	54	<i>a, b, d, e</i>	3440-3360-3100	C <sub>8</sub> H <sub>14</sub> N <sub>2</sub> SCu	Cu, 31.96	Cu, 32.8
<i>n</i> -C <sub>4</sub> H <sub>9</sub>	H	175	86	<i>a, c, g</i>	3420-3320-3160	C <sub>9</sub> H <sub>18</sub> N <sub>2</sub> SCu	Cu, 31.47	Cu, 30.3
<i>n</i> -C <sub>6</sub> H <sub>13</sub>	H	155	96	<i>a, c, d, e</i>	3450-3270-3120	C <sub>13</sub> H <sub>22</sub> N <sub>2</sub> SCu	C, 38.8 H, 6.7 N, 17.2 S, 13.2	C, 38.3 H, 6.4 N, 16.8 S, 12.8
<i>n</i> -C <sub>7</sub> H <sub>15</sub>	H	153	98	<i>a, c, d</i>	3440-3270-3100	C <sub>15</sub> H <sub>26</sub> N <sub>2</sub> SCu	Cu, 25.4 C, 41.11 H, 7.31 N, 15.80 S, 12.40	Cu, 25.35 C, 41.0 H, 6.83 N, 15.92 S, 12.13
<i>n</i> -C <sub>8</sub> H <sub>17</sub>	H	150	91	<i>a, c, d</i>	3450-3280-3110	C <sub>16</sub> H <sub>28</sub> N <sub>2</sub> SCu	Cu, 24.3 C, 44.37 H, 7.89 N, 15.10 S, 11.48	Cu, 24.4 C, 43.3 H, 7.22 N, 15.10 S, 11.95
<i>n</i> -C <sub>9</sub> H <sub>19</sub>	H	149	98	<i>a, c, d</i>	3420-3270-3100	C <sub>17</sub> H <sub>30</sub> N <sub>2</sub> SCu	Cu, 23.0 N, 13.98 S, 10.63	Cu, 22.85 N, 14.4 S, 10.98
<i>n</i> -C <sub>10</sub> H <sub>21</sub>	H	148	84	<i>a, c, d</i>	3450-3280-3105	C <sub>18</sub> H <sub>32</sub> N <sub>2</sub> SCu	Cu, 21.42 C, 46.97 H, 7.92 N, 14.56 S, 11.08	Cu, 21.75 C, 47.2 H, 7.86 N, 13.72 S, 10.5
<i>n</i> -C <sub>11</sub> H <sub>23</sub>	H	146	88	<i>a, c, d</i>	3440-3280-3100	C <sub>19</sub> H <sub>34</sub> N <sub>2</sub> SCu	Cu, 19.9 C, 49.46 H, 8.07 N, 13.41 S, 10.28	Cu, 20.8 C, 48.8 H, 8.14 N, 13.13 S, 10.10
<i>n</i> -C <sub>13</sub> H <sub>27</sub>	CH <sub>3</sub>	134	88	<i>a, c, d</i>	3480-3330-3190	C <sub>21</sub> H <sub>38</sub> N <sub>2</sub> SCu	Cu, 19.9 C, 50.55 H, 8.81 N, 12.20 S, 9.57	Cu, 19.86 C, 50.4 H, 8.4 N, 12.58 S, 9.60
<i>n</i> -C <sub>15</sub> H <sub>31</sub>	CH <sub>3</sub>	127	78	<i>a, c, d</i>	3460-3320-3180	C <sub>23</sub> H <sub>40</sub> N <sub>2</sub> SCu	Cu, 18.9 C, 55.64 H, 9.29 N, 10.95 S, 8.33	Cu, 19.0 C, 55.5 H, 9.24 N, 10.8 S, 8.23
CH <sub>2</sub> —CH <sub>2</sub> —CH <sub>2</sub> —CH <sub>2</sub> —CH <sub>2</sub> —		165	83	<i>a, c, d</i>	3410-3280-3160	C <sub>7</sub> H <sub>14</sub> N <sub>2</sub> SCu	Cu, 16.4 C, 34.61 H, 5.43 N, 17.92 S, 13.92	Cu, 16.3 C, 35.8 H, 5.5 N, 17.91 S, 13.64
CH=CH=CH—C—   O	H	191	75	<i>a, c, g</i>	3460-3350	C <sub>6</sub> H <sub>7</sub> N <sub>2</sub> OSC <sub>2</sub>	Cu, 26.66 C, 31.1 H, 3.0 N, 18.15 S, 13.68	Cu, 27.0 C, 31.1 H, 2.6 N, 18.14 S, 13.82
C <sub>6</sub> H <sub>5</sub>	H	183	60	<i>a, c, h, i</i>	3460-3360	C <sub>8</sub> H <sub>9</sub> N <sub>2</sub> SCu	Cu, 26.9 C, 39.88 H, 3.33 N, 17.4 S, 12.80	Cu, 27.0 C, 39.6 H, 3.7 N, 17.3 S, 13.1
<i>o</i> -OHC <sub>6</sub> H <sub>4</sub>	H	218	71	<i>a, c, d</i>	3450-3300	C <sub>8</sub> H <sub>7</sub> N <sub>2</sub> OSC <sub>2</sub>	Cu, 25.6 C, 36.65 H, 3.68 N, 16.40 S, 12.05	Cu, 26.2 C, 37.2 H, 3.1 N, 16.3 S, 12.4
							Cu, 24.45	Cu, 24.5

TABLE II (Concluded)

Thiosemicarbazone-copper complexes:  $\left( \begin{array}{c} \text{Y}-\text{C}=\text{N}-\text{NH}-\text{C}-\text{NH}_2 \\ | \quad \quad \quad || \\ \text{X} \quad \quad \quad \text{S} \end{array} \right) \text{Cu}$

Y	X	M.p., °C	Yield	Methods of purifica- tion	Typical I.R. absorptions in the —NH— region, cm <sup>-1</sup>	Formula	Found, %	Calculated, %
<i>m</i> -OHC <sub>6</sub> H <sub>4</sub>	H	187	88	<i>a, c, d, e</i>	3400-3290	C <sub>8</sub> H <sub>8</sub> N <sub>4</sub> OSC <sub>6</sub> H <sub>4</sub>	N, 15.85 S, 12.15	N, 16.3 S, 12.4
<i>p</i> -OHC <sub>6</sub> H <sub>4</sub>	H	>300	60	<i>a, b, c, d, e</i>	3460-3340	C <sub>8</sub> H <sub>8</sub> N <sub>4</sub> OSC <sub>6</sub> H <sub>4</sub>	Cu, 24.43 N, 16.5 S, 12.78	Cu, 24.5 N, 16.3 S, 12.4
<i>m</i> -O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub>	H	224	75	<i>a, c, d, e</i>	3480-3370	C <sub>8</sub> H <sub>7</sub> N <sub>4</sub> O <sub>2</sub> SC <sub>6</sub> H <sub>4</sub>	Cu, 22.9 C, 33.15 H, 2.53 N, 18.50 S, 10.7	Cu, 24.5 C, 33.5 H, 2.44 N, 19.5 S, 11.17
<i>o</i> -FC <sub>6</sub> H <sub>4</sub>	H	171	88	<i>a, c, h</i>	3430-3320	C <sub>8</sub> H <sub>7</sub> FN <sub>4</sub> SC <sub>6</sub> H <sub>4</sub>	Cu, 22.23 C, 36.53 H, 3.4 N, 16.15 S, 12.25	Cu, 22.15 C, 37.0 H, 2.7 N, 16.2 S, 12.34
<i>m</i> -FC <sub>6</sub> H <sub>4</sub>	H	171	50	<i>a, c, h</i>	3440-3330	C <sub>8</sub> H <sub>7</sub> FN <sub>4</sub> SC <sub>6</sub> H <sub>4</sub>	Cu, 24.5 C, 37.33 H, 3.25 N, 15.96 S, 12.20	Cu, 24.5 C, 37.0 H, 2.7 N, 16.2 S, 12.34
<i>p</i> -FC <sub>6</sub> H <sub>4</sub> <sup>a</sup>	H	172	50	<i>a, c, h</i>	3450-3340	C <sub>8</sub> H <sub>7</sub> FN <sub>4</sub> SC <sub>6</sub> H <sub>4</sub>	Cu, 23.9 Cu, 23.0	Cu, 24.5 Cu, 24.5
<i>o</i> -ClC <sub>6</sub> H <sub>4</sub>	H	195	91	<i>a, c, g</i>	3490-3360	C <sub>8</sub> H <sub>7</sub> ClN <sub>4</sub> SC <sub>6</sub> H <sub>4</sub>	C, 34.8 H, 2.9 Cl, 13.2 N, 15.6 S, 12.1	C, 34.8 H, 2.5 Cl, 12.9 N, 15.2 S, 11.6
<i>p</i> -ClC <sub>6</sub> H <sub>4</sub>	H	188	86	<i>a, c, g, j</i>	3480-3360	C <sub>8</sub> H <sub>7</sub> ClN <sub>4</sub> SC <sub>6</sub> H <sub>4</sub>	Cu, 22.9 C, 34.1 H, 2.8 Cl, 12.4 N, 15.0 S, 11.15	Cu, 22.9 C, 34.8 H, 2.5 Cl, 12.9 N, 15.2 S, 11.6
<i>p</i> -(OCH <sub>3</sub> )C <sub>6</sub> H <sub>4</sub>	H	183	93	<i>a, c, d</i>	3460-3330	C <sub>9</sub> H <sub>10</sub> N <sub>4</sub> OSC <sub>6</sub> H <sub>4</sub>	Cu, 22.8 N, 15.52 S, 12.30	Cu, 22.9 N, 15.45 S, 11.8
2,5-OH(Cl)C <sub>6</sub> H <sub>3</sub>	H	>300	89	<i>a, c, d</i>	3430-3280	C <sub>8</sub> H <sub>7</sub> ClN <sub>4</sub> OSC <sub>6</sub> H <sub>4</sub>	Cu, 22.5 C, 32.16 H, 2.97 Cl, 12.20 N, 14.15 S, 10.67	Cu, 23.4 C, 32.82 H, 2.39 Cl, 12.17 N, 14.38 S, 10.96
2,4-(Cl) <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	H	204	100	<i>a, c, d, h</i>	3480-3360	C <sub>8</sub> H <sub>5</sub> Cl <sub>2</sub> N <sub>4</sub> SC <sub>6</sub> H <sub>4</sub>	Cu, 21.3 C, 29.9 H, 2.00 Cl, 22.66 N, 13.28 S, 10.20	Cu, 21.75 C, 30.8 H, 1.93 Cl, 22.80 N, 13.49 S, 10.28
<i>p</i> -ClC <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub>	165	88	<i>a, c, g, h</i>	3410-3260	C <sub>8</sub> H <sub>9</sub> ClN <sub>4</sub> SC <sub>6</sub> H <sub>4</sub>	Cu, 19.9 C, 37.20 H, 3.97 Cl, 14.10 N, 15.05 S, 11.53	Cu, 20.4 C, 37.25 H, 3.10 Cl, 12.25 N, 14.5 S, 11.05
C <sub>6</sub> H <sub>5</sub> CH(OH)	C <sub>6</sub> H <sub>5</sub>	216	20	<i>c</i>	3460-3260-3140	C <sub>10</sub> H <sub>14</sub> N <sub>4</sub> OSC <sub>6</sub> H <sub>4</sub>	Cu, 20.8 C, 50.7 H, 3.7 N, 12.3 S, 9.3	Cu, 21.8 C, 51.8 H, 3.75 N, 12.2 S, 9.24
							Cu, 18.6	Cu, 18.3

<sup>a</sup>Washed with hydrochloric acid 3%.<sup>b</sup>Washed with hydrochloric acid 10%.<sup>c</sup>Washed with boiling methyl alcohol.<sup>d</sup>Washed with boiling acetone.<sup>e</sup>Washed with boiling benzene.<sup>f</sup>Washed with dilute ammonium hydroxide.<sup>g</sup>Dissolved in acetone and recovered by evaporation of the solvent.<sup>h</sup>Crystallized from acetone.<sup>i</sup>Crystallized from aqueous cellosolve.<sup>j</sup>Crystallized from aqueous dioxan.<sup>k</sup>Crystallized from aqueous acetone.<sup>l</sup>Not enough material for complete analysis.



In the case of the aromatic hydroxy compounds, it is also possible that the hydroxyl groups are involved in the metal binding process, since their infrared spectra do not show a band in the OH region.

More work is being done at the moment on the structure of those copper complexes.

Although a full discussion of the microbiological data will appear elsewhere (18), it is interesting to note that antifungal activity is restricted to the thiosemicarbazones themselves, most of the copper complexes being found inactive.

#### EXPERIMENTAL

Carbonyl compounds were obtained from commercial sources except in the case of the four fluorobenzaldehydes which were prepared from the corresponding fluorotoluenes by Etard's reaction (21). Thiosemicarbazones were prepared by the method of Sah and Daniels (19). Copper complexes were made by a method similar to that used by Kuhn and Zilliken (15) using cuprous chloride in ammonium hydroxide. 2-Methylthiosemicarbazide (III) and its benzylidene derivative (IV) were made by the method of Greer and Smith (20). Melting points, yields, solvents used in purification, bands in the  $\text{—NH—}$  region of the infrared spectrum, and analyses are reported in Tables I and II. Melting points were taken on a Fisher-John apparatus and are not corrected.

##### *o*-Fluorobenzaldehyde Thiosemicarbazone

*o*-Fluorobenzaldehyde was first prepared using 40 g (0.36 mole) *o*-fluorotoluene (from *o*-toluidine; b.p.  $114^\circ$ , lit. b.p.  $114^\circ$ ) (22) in glacial acetic acid (570 ml), acetic anhydride (565 ml), concentrated sulphuric acid (85 ml), and chromium trioxide (100 g). There was obtained *o*-fluorobenzaldiacetate (18 g, 40%, m.p.  $25\text{--}27^\circ$ ), which was hydrolyzed to the free aldehyde by heating under reflux for  $\frac{1}{2}$  hour in a mixture of ethyl alcohol (50 ml), water (25 ml), and sulphuric acid (10 ml). A sample of the resulting solution treated with phenylhydrazine afforded *o*-fluorobenzaldehyde phenylhydrazone (m.p.  $89^\circ$ , lit. m.p.  $89.5^\circ$ ) (23).

The rest of the solution was neutralized to litmus and to this was added a solution of thiosemicarbazide (I) (9.1 g, 0.1 mole) in water (150 ml) and acetic acid (10 ml). *o*-Fluorobenzaldehyde thiosemicarbazone (II,  $Y = \text{o-FC}_6\text{H}_4$ ,  $X = \text{H}$ ) crystallized at once.

##### *m*-Fluorobenzaldehyde Thiosemicarbazone

*m*-Fluorobenzaldehyde was prepared by the same method using *m*-fluorotoluene (31.5 g, 0.28 mole; from *m*-toluidine; b.p.  $116^\circ$ , lit. b.p.  $116^\circ$ ) (22). The *m*-fluorobenzaldiacetate obtained had m.p.  $37^\circ$  (18 g, 27%). Anal. calc. for  $\text{C}_{11}\text{H}_{11}\text{FO}_4$ : mol. wt., 226; C, 58.4; H, 4.9. Found: C, 59.1; H, 5.7.

Hydrolysis of the latter with sulphuric acid (10 ml) in aqueous alcohol gave a solution of *m*-fluorobenzaldehyde. A portion of this solution, reacted with phenylhydrazine to give the expected phenylhydrazone (m.p.  $113^\circ$ , lit. m.p.  $114^\circ$ ) (22). After neutralization, the remaining solution was mixed with 300 ml of an aqueous solution of thiosemicarbazide (9.1 g, 0.1 mole) and the thiosemicarbazone crystallized immediately.

##### *p*-Fluorobenzaldehyde Thiosemicarbazone

This preparation was carried out as above using *p*-fluorotoluene (11.7 g, 0.1 mole; b.p.  $116^\circ$ , lit. b.p.  $117^\circ$ ) (22) from *p*-toluidine). The diacetate did not crystallize in this case but was extracted with ether. After evaporation of the solvent, the residual oil was hydrolyzed in the usual manner and its reaction with thiosemicarbazide gave the expected thiosemicarbazone.

*2-Fluoro-5-nitrobenzaldehyde Thiosemicarbazone*

This compound was prepared as the previous ones starting with 2-fluoro-5-nitrotoluene (24) (40 g, 0.24 mole). The diacetate was obtained as an uncrystallizable oil (26 g, 38%), which after hydrolysis and reaction with thiosemicarbazide gave the expected thiosemicarbazone.

*Preparation of Copper Complexes*

The preparation of benzaldehyde thiosemicarbazone - copper complex illustrates the general method used.

To a gently refluxing solution of benzaldehyde thiosemicarbazone (9.8 g, 0.05 mole) in methyl alcohol (200 ml) was added dropwise a solution of cuprous chloride (5 g, 0.05 mole) in ammonium hydroxide (100 ml, sp. gr. 0.9). A yellow precipitate was formed and the mixture was stirred for  $\frac{1}{2}$  hour to complete the formation of the complex. After cooling, the solid was collected by filtration and washed with dilute hydrochloric acid, water, and alcohol.

Other purifying procedures are listed, for each compound, in Table II.

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# DISTRIBUTION OF SUBSTITUENTS IN A PARTIALLY METHYLATED 4-O-METHYLGLUCURONOXYLAN<sup>1</sup>

INGEMAR CROON<sup>2</sup> AND T. E. TIMELL

## ABSTRACT

A 4-O-methylglucuronoxylan has been partially methylated and the distribution of the substituents has been established. The hydroxyl group at C<sub>3</sub> was less reactive than that at C<sub>2</sub> in both the main xylan chain and in the acid side chains. Caution should be exercised in attributing structural significance to the presence of small amounts of sugars containing C<sub>3</sub> hydroxyl groups in hydrolyzates from methylated xyans.

In a previous investigation (1) the distribution of the substituents in a partly methylated xylan from esparto grass was established. This paper is concerned with the location of the substituents in a partially methylated 4-O-methylglucuronoxylan from white birch wood, a type of xylan more frequently encountered than the neutral polymer occurring in esparto.

## RESULTS AND DISCUSSION

The polysaccharide was isolated by alkaline extraction of a birch chlorite holocellulose (2). It had previously (3) been found to contain 120 (1 → 4)-linked β-D-xylopyranose residues in a linear chain to which single side chains of 4-O-methyl-α-D-glucuronic acid residues were attached through C<sub>2</sub> of every tenth, on the average, of the xylose residues. The xylan was methylated with dimethyl sulphate and alkali until a methoxyl content of 26.6% had been reached. The partly methylated product was subjected to methanolysis and neutral and acidic sugars were separated on a column of anion exchange resin. The acid portion contained as sole component a partly methylated aldobiouronic acid, composed of xylose and glucuronic acid residues. It was esterified, reduced, and hydrolyzed to yield a mixture of reducing sugars. Hydrolysis of the neutral fraction gave a similar sugar mixture.

Both mixtures were separately resolved on a column of charcoal and Celite (4) by gradient elution (5) with aqueous ethanol (6). With one exception, complete resolution was achieved throughout. All sugars were either obtained crystalline or were converted to crystalline derivatives. The results are presented in Table I.

TABLE I  
Molar composition in percentage of neutral and acid portions of the  
4-O-methylglucuronoxylan

Neutral portion		Acid portion	
D-Xylose	10.6	D-Xylose	7.8
2-O-Methyl-D-xylose	12.3	3-O-Methyl-D-xylose	39.5
3-O-Methyl-D-xylose	9.8	4-O-Methyl-D-glucose	5.9
2,3-Di-O-methyl-D-xylose	67.3	2,4-Di-O-methyl-D-glucose	7.0
		3,4-Di-O-methyl-D-glucose	3.4
		2,3,4-Tri-O-methyl-D-glucose	36.4

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<sup>2</sup>Harold Hibbert Memorial Fellow, McGill University, 1959.

In the case of the esparto xylan, a direct comparison between found and statistically calculated distributions (1) showed that the C<sub>2</sub> hydroxyl group was approximately 2.5 times as reactive as the C<sub>3</sub> hydroxyl but that methylation at C<sub>2</sub> doubled the reactivity of the remaining C<sub>3</sub> hydroxyl (7). Such a calculation is less easily applied in the present case. It is evident, however, that in those xylose residues in the main chain which carried no acid side groups, the ratio between the relative reactivities of the C<sub>2</sub> and C<sub>3</sub> hydroxyl groups was lower than the corresponding value for the esparto xylan. The distribution of the C<sub>2</sub> and C<sub>3</sub> methoxyl groups in the acid side chains corresponded to that expected for a partly methylated polysaccharide containing two hydroxyl groups, one of which was two to three times as reactive as the other. Those xylose residues which carried side chains were almost completely substituted.

The results indicate that the C<sub>2</sub> hydroxyl group is more reactive than that at C<sub>3</sub> in both the main xylan chain and in the side chains of a 4-O-methylglucuronoxylan. Due to changes in the electron density distribution (1, 7), the reactivity of the C<sub>3</sub> hydroxyl is probably enhanced by substitution at C<sub>2</sub>. Complete methylation of polysaccharides is sometimes extremely difficult to achieve. It is clear from the present results that incomplete methylation is likely to cause the presence of mainly 2-O-methyl-D-xylose and 2,4-di-O-methyl-D-glucuronic acid in the acid hydrolyzate of 4-O-methylglucuronoxylans. Caution should be exercised in attributing structural significance to these sugars, even in the absence of the corresponding 3-O- and 3,4-di-O-substituted derivatives.

#### EXPERIMENTAL

Specific rotations were equilibrium values and were determined at a temperature of +25° C, at a concentration of 2.0, and with water as solvent. All melting points are corrected. Paper chromatography was carried out with a butan-2-one-water mixture (89:11) and sugars were located by spraying with *o*-aminodiphenyl (8). Paper electrophoresis was carried out with a 0.05 *M* borate buffer at a pH of 9.4.

##### *Methylation of the Hemicellulose*

A 4-O-methylglucuronoxylan was prepared in 29% yield (based on the wood) from a white birch chlorite holocellulose (2). The hemicellulose gave only xylose and uronic acids on hydrolysis and had a number-average degree of polymerization of 120 (osmometry). 4-O-Methylglucuronoxylan (25 g) was dissolved in 24% (w/w) potassium hydroxide (600 ml) in an atmosphere of nitrogen, and dimethyl sulphate (400 ml) was added dropwise at room temperature over a period of 18 hours. The reaction mixture was neutralized with acetic acid and was dialyzed against distilled water for a week. Freeze-drying of the solution gave a white, fluffy material (22 g), OMe, 26.6%.

##### *Methanolysis and Separation of Neutral and Acidic Sugars*

The partly methylated hemicellulose (21.5 g) was boiled under reflux for 10 hours with 2% methanolic hydrogen chloride in the presence of Drierite. Neutralization with silver carbonate, filtration through Celite, and evaporation to dryness yielded a pale, yellow sirup (21 g). The mixture of glycosides was dissolved in water (200 ml) and treated with barium hydroxide (10 g) at 70° for 2 hours (9). Excess barium carbonate was removed by addition of solid carbon dioxide, followed by filtration through Celite, after which the solution was treated with Amberlite IR-120 exchange resin and concentrated to 200 ml. The acidic solution was added to the top of a column (5×30 cm) containing Dowex 1-X4 exchange resin (20–50 mesh, acetate cycle). Neutral sugars

(15.2 g) were eluted with water (5–6 liters), after which an acid fraction (2.5 g) was obtained by elution with 30% aqueous acetic acid (4 liters).

#### *Reduction of the Acid Fraction and Hydrolysis of the Glycosides*

The acid fraction was boiled under reflux with 2% methanolic hydrogen chloride and the ester-glucoside mixture was reduced with lithium aluminum hydride (2.5 g) in dry tetrahydrofuran (100 ml). Hydrolysis of the neutral fraction and of the reduced acid fraction yielded two mixtures of reducing sugars (A and B, respectively).

#### *Resolution of Sugar Mixture A*

A portion of the mixture of neutral sugars (A) (1.55 g) was added to the top of a Darco G-60 charcoal – Celite column (4) (1:1 w/w, 3.5×55 cm) and the sugars were recovered by gradient elution with aqueous ethanol as described previously (1). Four fractions containing only one compound were obtained, in addition to one which was a mixture of mono-*O*-methylxyloses and which was further resolved by paper electrophoresis. Amount recovered: 1.41 g.

#### *Identification of Sugars*

*D-Xylose*.—The first fraction (131 mg) crystallized, m.p. and mixed m.p. 145–146° C,  $[\alpha]_D +19^\circ$ .

*3-O-Methyl-D-xylose*.—This sugar (132 mg) also crystallized, m.p. and mixed m.p. 102–103° C,  $[\alpha]_D +18^\circ$ .

*2-O-Methyl-D-xylose*.—The crystalline sugar (166 mg) had m.p. and mixed m.p. 133–134° C,  $[\alpha]_D +36^\circ$ .

*2,3-Di-O-methyl-D-xylose*.—This sugar which constituted the last fraction (982 mg) had m.p. 101° C after recrystallization from ethyl acetate (10, 11),  $[\alpha]_D +22^\circ$ .

#### *Resolution of Sugar Mixture B*

Sugar mixture B (2.2 g) was added to the top of the same charcoal–Celite column and successively eluted with the following solvents: water (3 liters) → 10% ethanol (3 liters), 10% ethanol (2 liters) → 20% ethanol (2 liters), 20% ethanol (1 liter) → 50% ethanol (1 liter). The total amount of material recovered was 2.0 g.

#### *Identification of Sugars*

*D-Xylose*.—The first fraction (124 mg) crystallized, m.p. and mixed m.p. 145° C,  $[\alpha]_D +18^\circ$ .

*3-O-Methyl-D-xylose*.—The crystalline sugar (671 mg) had m.p. and mixed m.p. 102–103° C,  $[\alpha]_D +18^\circ$ .

*4-O-Methyl-D-xylose*.—The sirupy sugar (121 mg),  $[\alpha]_D +61^\circ$ , was converted to its crystalline osazone, m.p. and mixed m.p. 157–158° C. Its infrared spectrum was identical with that of an authentic specimen.

*2,4-Di-O-methyl-D-glucose*.—This fraction was contaminated with an unknown compound, travelling faster on the paper chromatogram. The mixture (168 mg) was added to the top of a cellulose column (3.8×35 cm) and eluted with butan-2-one saturated with water to yield a pure di-*O*-methylglucose (154 mg). The sirupy sugar,  $[\alpha]_D +76^\circ$ , was converted to the crystalline 2,4-di-*O*-methyl-*N-p*-nitrophenyl-*D*-glucosylamine, m.p. 250–251° C, undepressed on admixture with an authentic sample.

*3,4-Di-O-methyl-D-glucose*.—The crystalline sugar (76 mg) had m.p. and mixed m.p. 113–115° C,  $[\alpha]_D +95^\circ$ .

*2,3,4-Tri-O-methyl-D-glucose*.—The sirupy sugar (860 mg),  $[\alpha]_D +65^\circ$ , was converted to the crystalline 2,3,4-tri-*O*-methyl-*N*-phenyl-*D*-glucosylamine, m.p. and mixed m.p. 144–145° C.

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# ELECTRON SPIN RESONANCE ABSORPTION OF DIPHENYLPICRYLHYDRAZYL - ZINC OXIDE MIXTURES<sup>1</sup>

Y. MATSUNAGA<sup>2</sup> AND C. A. McDOWELL

## ABSTRACT

Electron spin resonance measurements on mixtures of  $\alpha\alpha$ -diphenyl- $\beta$ -picrylhydrazyl (DPPH) and zinc oxide when compared with corresponding determinations on DPPH itself, and with DPPH - potassium chloride mixtures, indicate that there is a transfer of electrons between the DPPH and the zinc oxide. These observations support earlier published views of Harrison and McDowell, who found that the above mixture was able to enhance the catalysis of the ortho-para hydrogen conversion, and the hydrogen-deuterium exchange reaction.

## INTRODUCTION

Mixtures of  $\alpha\alpha$ -diphenyl- $\beta$ -picrylhydrazyl (DPPH) and zinc oxide have been found to be more efficient catalysts of the ortho-para hydrogen conversion (1, 2) than either of the two components alone. This led Harrison and McDowell (2) to postulate that the enhancement of the catalysis was caused by an electron transfer process occurring at the DPPH - zinc oxide interface. More recently Eley and Inokuchi (3) have found evidence for partial transfer processes in the systems DPPH-hydrogen, and also in DPPH - hydrogen sulphide. We here report the results of some experiments on the electron spin resonance absorption of mixtures of DPPH and potassium chloride, and DPPH and zinc oxide. These observations, as do also some less complete ones on DPPH - nickel oxide mixtures, confirm the earlier views of Harrison and McDowell (2) that electron transfer processes occur at the DPPH - zinc oxide interface.

## EXPERIMENTAL

Pure non-sintered zinc oxide was prepared by treating a slightly acidic solution of zinc sulphate with metallic zinc to remove heavy metal ions. Ferrous iron was oxidized with hydrogen peroxide and removed by coprecipitation with zinc hydroxide by addition of a small quantity of ammonium hydroxide solution. Zinc oxalate was prepared from thus purified solution of zinc sulphate and calcined at 400° C for 6 hours.

$\alpha\alpha$ -Diphenyl- $\beta$ -picrylhydrazyl (DPPH) was prepared by oxidation of the corresponding hydrazine, supplied by Eastman-Kodak, with lead dioxide and recrystallized from a mixture of benzene and ligroin. Our sample contained crystalline benzene, but the mole ratio is less than one (6). Therefore, there is to be expected an "oxygen effect" as reported by Bennett and Morgan (5).

DPPH and zinc oxide mixtures were prepared, in a ratio of 1:9 by weight, by grinding the compounds in a mortar. The derivative of the electron spin resonance absorption was recorded on our electron spin resonance spectrometer at a frequency of 9000 Mc/sec. For convenience the distance between points of maximum slope  $\Delta H_{ms}$  and the peak-to-peak intensity  $I_p$  on derivative curve will be used in this paper. The area  $A$  under the absorption curve can be estimated by the product of the square of  $\Delta H_{ms}$  and  $I_p$  (3). The value of  $I_p$  of DPPH in vacuum is taken as unity.

## RESULTS AND DISCUSSION

The DPPH used in this experiment had a  $\Delta H_{ms}$  of 1.4 oersteds *in vacuo*, and a  $\Delta H_{ms}$  of 1.45 oersteds and an  $I_p$  of 0.66 in air. The value of  $\Delta H_{ms}$  of crystalline solvent-free DPPH

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has been reported to be 0.85 oersted and that with 0.8 mole of crystalline benzene 4.6 oersteds (3). No electron spin resonance absorption was detected in zinc oxide under the conditions of the present experiments.

A preliminary examination of the interaction between DPPH and zinc oxide was carried out in air without considering the oxygen effect. By grinding the compounds for a few minutes the value of  $I_p$  decreased to less than 0.4. A further, more rapid, decrease in  $I_p$  was caused by prolonged mixing.  $I_p$  was also observed to decrease slowly on standing. These results are shown in Fig. 1.

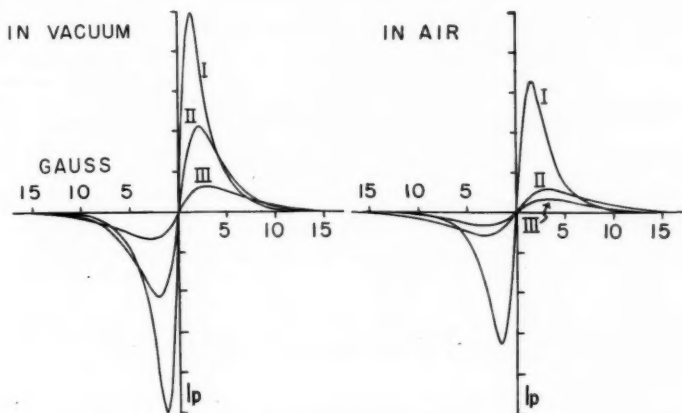


FIG. 1. Electron spin resonance absorption of mixtures of diphenylpicrylhydrazyl and zinc oxide. Curve I refers to DPPH alone; curve II refers to the DPPH-ZnO mixture No. 2 in Table I; curve III refers to the DPPH-ZnO mixture No. 4 in Table I. The value of  $I_p$  for DPPH in vacuum is taken as unity.

The variation of  $I_p$  with time is shown in Fig. 2. Curves A and B in this figure refer to measurements on the same mixture but at different degrees of mixing. Although the  $I_p$  of DPPH shows a marked decrease by grinding with zinc oxide, the area under the

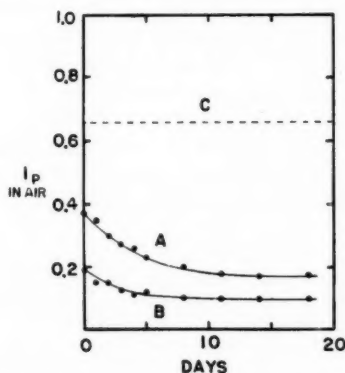


FIG. 2. Variation of the electron spin resonance absorption of mixtures of diphenylpicrylhydrazyl and zinc oxide (1:9) with time. Curves A and B refer to two mixtures with different degrees of admixing (B is the result of prolonged mixing). Curve C refers to a mixture of diphenylpicrylhydrazyl and potassium chloride (1:9); DPPH alone also gives a signal of this magnitude.

absorption curve, which is proportional to the electron spin concentration, does not change so much because of the increase of  $\Delta H_{ms}$ . No change of  $g$ -value was observed.

The results shown in Figs. 1 and 2 indicate that the values of  $\Delta H_{ms}$  and  $I_p$  mixtures of DPPH and potassium chloride (1:9) do not change with time, nor do these data differ from the values for DPPH alone. Therefore, the observed line broadening in DPPH - zinc oxide mixtures suggests that there is a change of environment of the unpaired electrons by some kind of interaction between the DPPH and the zinc oxide. As this solid-solid interaction proceeds fairly rapidly by grinding, it was found quite difficult to prepare homogeneously mixed samples in different stages of the interaction. A few preparations, which could be considered to be well mixed, were examined *in vacuo* and in air. The results are given in the following table.

TABLE I  
Electron spin resonance absorption of DPPH-ZnO mixtures

	In vacuum			In air		
	$\Delta H_{ms}$	$I_p$	$A^*$	$\Delta H_{ms}$	$I_p$	$A^*$
DPPH-KCl	1.4	1.00	1.0	1.45	0.66	0.7
DPPH-ZnO (1)	1.85	0.63	1.1	2.5	0.22	0.7
(2)	2.1	0.43	1.0	3.2	0.12	0.6
(3)	2.2	0.31	0.8	3.2	0.10	0.5
(4)	2.85	0.13	0.5	3.5	0.07	0.4

NOTE: The numbers, for example (1), after the DPPH-ZnO refer to different mixtures.

\*Estimated error  $\pm 0.1$ .

The data obtained *in vacuo* show that the absorption line is broadened by interaction between DPPH and zinc oxide. The electron spin concentration seems to be constant in the initial stages of mixing, but a permanent decrease is found as time increases. It is not clear whether this apparent loss of spin is due to the real disappearance of unpaired electrons or the fact that some of unpaired electrons are in a different state and show too broad a resonance absorption to be detected. It is, however, apparent that there is some transfer of electrons, though whether this transfer is from the DPPH to the zinc oxide, or vice versa, cannot be deduced from our results.

The decrease of  $I_p$  by admission of air is several times larger in DPPH - zinc oxide mixtures than in DPPH alone. This oxygen effect on electron spin resonance absorption is instantaneous and reversible in DPPH (2) and also in DPPH - zinc oxide.

Since zinc oxide is an excess, or  $n$ -type, semiconductor, it was of interest to see if the effects observed with mixtures of this compound and DPPH would also occur with a defect, or  $p$ -type, semiconductor and DPPH. A few experiments were carried out with DPPH and nickel oxide which is a  $p$ -type semiconductor. The nickel oxide was prepared by calcination of the nitrate. The results are shown in Table II.

TABLE II  
Electron spin resonance absorption of DPPH-NiO mixtures

	In vacuum			In air		
	$\Delta H_{ms}$	$I_p$	$A^*$	$\Delta H_{ms}$	$I_p$	$A^*$
DPPH-CCl	1.4	1.00	1.0	1.45	0.66	0.7
DPPH-NiO (1)	1.7	0.22	0.3	2.0	0.18	0.4
(2)	2.8	0.045	0.2	3.1	0.036	0.2

The same trends are observed in the results for the DPPH - nickel oxide mixtures as we found for the DPPH - zinc oxide mixtures. These observations must, therefore, be taken as additional evidence that electron transfer processes do occur at DPPH-oxide interfaces.

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# THE STUDY OF HYDROGEN BONDING AND RELATED PHENOMENA BY ULTRAVIOLET LIGHT ABSORPTION

## PART III. THE STRENGTH OF THE DIMERIC HYDROGEN BOND IN SUBSTITUTED BENZOIC ACIDS AS A MEASURE OF ELECTRONIC AND STERIC INTERACTIONS<sup>1</sup>

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### ABSTRACT

The strength of the intermolecular (dimeric) hydrogen bond in substituted benzoic acids, as estimated from the observed concentration dependence of the ultraviolet absorption spectra, is found to vary with the nature and the position of the substituent. The effects of a number of substituents on the strength of the dimeric hydrogen bond can be rationalized in terms of the usual electronic and steric interactions. The data indicate that *o*-methoxybenzoic acid forms a stronger intramolecular hydrogen bond than *o*-fluorobenzoic acid.

### INTRODUCTION

In Part II (1) it was shown that the observed concentration dependences of the main absorption band in the ultraviolet spectra for a number of benzoic acids could be satisfactorily explained by supposing that these changes are caused by the effect of dilution on the benzoic acid monomer-dimer equilibrium. The greatest concentration at which a marked concentration dependence is first observed was taken as an approximate measure of the dimeric bond strength. This "critical" concentration was greater when the intermolecular hydrogen bond was assumed to be weak than if the bond was assumed to be strong. The purpose of the present paper is to summarize the available concentration dependences and to compare these values with other available data.

### EXPERIMENTAL

The method of determining the ultraviolet spectra has been described in Part II (1), which also lists some of the relevant concentration dependences. Additional data are listed in Figs. 1, 3, and 4, and Table I lists all the available critical maximal concentrations and the infrared data.

Critical maximal concentrations were used for comparison purposes, rather than to attempt to obtain the dimerization constants, for the following reasons:

(i) It was found impossible to obtain a value of the extinction coefficient which could confidently be associated with the absorption of the monomeric form (see Figs. 1, 3, and 4, which show that no definite flattening out occurs at the left-hand side of the plots). Calculations using the accepted value of  $K_D$  ( $K_D = [D]/[M]^2$ ,  $[D]$  = concn. of dimer,  $[M]$  = concn. of monomer) indicate that the minimal critical concentrations should occur only at ca.  $10^{-6}$  M, which lies outside the investigated concentration range. This

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confirms the experimental observation that measurements for solutions containing only monomeric species cannot be obtained directly. Moreover, extrapolation to zero concentration of the observed curve to obtain the value corresponding to monomer absorption is considered unreliable since the curve does not obey exactly the relationship suggested by a simple monomer-dimer equilibrium (see below).

(ii) It was found impossible to obtain a reliable value for the absorption of the dimeric form. Although the absorption beyond the critical concentration remains approximately constant, this cannot be assumed to correspond to pure dimer absorption, since the infrared data indicate the presence of monomer even beyond this critical concentration (see Fig. 2). Using the accepted value for  $K_D$  of ca.  $1.6 \times 10^4$  for benzoic acid it was found that a theoretical plot of concentration against percentage of dimerized acid afforded a curve approximately but not entirely similar to that shown in Fig. 1, and that at the critical concentration the proportion of monomer would be ca. 82%. Comparison between the calculated and experimentally obtained curve for benzoic acid shows that only in the experimentally obtained curve is a critical maximal concentration dependence obtained. It is difficult to ascribe a reason for this behavior, but we can deduce from this

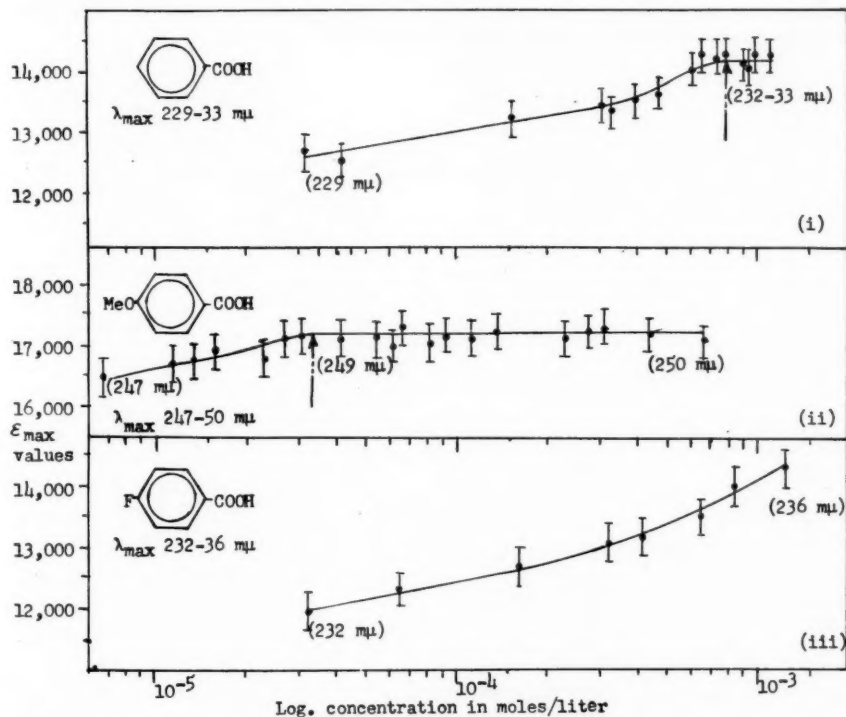


FIG. 1. The variation of  $\epsilon_{\max}$  on changing the solute concentration for (i) benzoic acid in cyclohexane solution, (ii) *p*-anisic acid in cyclohexane solution containing 5% ether,\* and (iii) *p*-fluorobenzoic acid in cyclohexane solution.

\*It has been shown (1) that the critical maximal concentration is not affected by small quantities of ether in solutions of cyclohexane.



that the observed relationship only approximates, but does not correspond exactly to, the simple mass action law relationship. It may also be noted that the infrared carbonyl spectra at concentrations within the solute concentration range  $0.5 \times 10^{-2}$  to  $0.5 M$ —that is above the "critical" level, where the ultraviolet absorption is constant—indicate that the dimer concentration still increases, but the monomer concentration significantly does *not* show a corresponding intensity decrease. This again is taken to indicate that deviations occur from the simple mass action law relationship.

Since the accurate absorption values of both the monomeric and dimeric form are required for the simple mass-law treatment, dimerization constants calculated from the simple mass action law using estimated values were found to afford a wide spread, although the values were approximately of the right order, that is, ranging between  $0.5 \times 10^{+4}$  to  $3.5 \times 10^{+4}$  for the value of  $K_D$ .

The infrared spectra at different solute concentrations were determined at  $30^\circ C$  in cyclohexane or carbon tetrachloride on a Unicam SP100 spectrophotometer in 0.5-mm cells, normally using a diffraction grating. Results are listed in Table I and Fig. 2. Figure 2 records the spectra in carbon tetrachloride solution because the lack of solubility of a number of acids in cyclohexane prevented the determination of the spectra in the latter solvent. However, when the acid was soluble in cyclohexane, the spectra were determined in both solvents and were found to be almost identical.

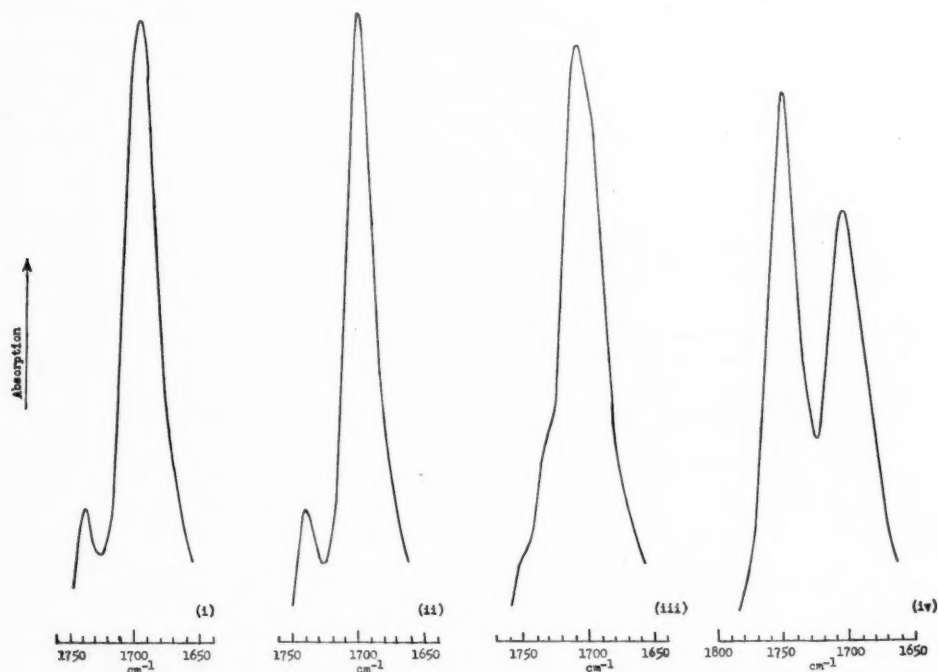


FIG. 2. The infrared carbonyl stretching bands in carbon tetrachloride solution at a concentration of ca.  $3.5 \times 10^{-2}$  moles/liter of (i) benzoic acid, (ii) *p*-fluorobenzoic acid, (iii) *o*-fluorobenzoic acid, and (iv) *o*-methoxybenzoic acid.

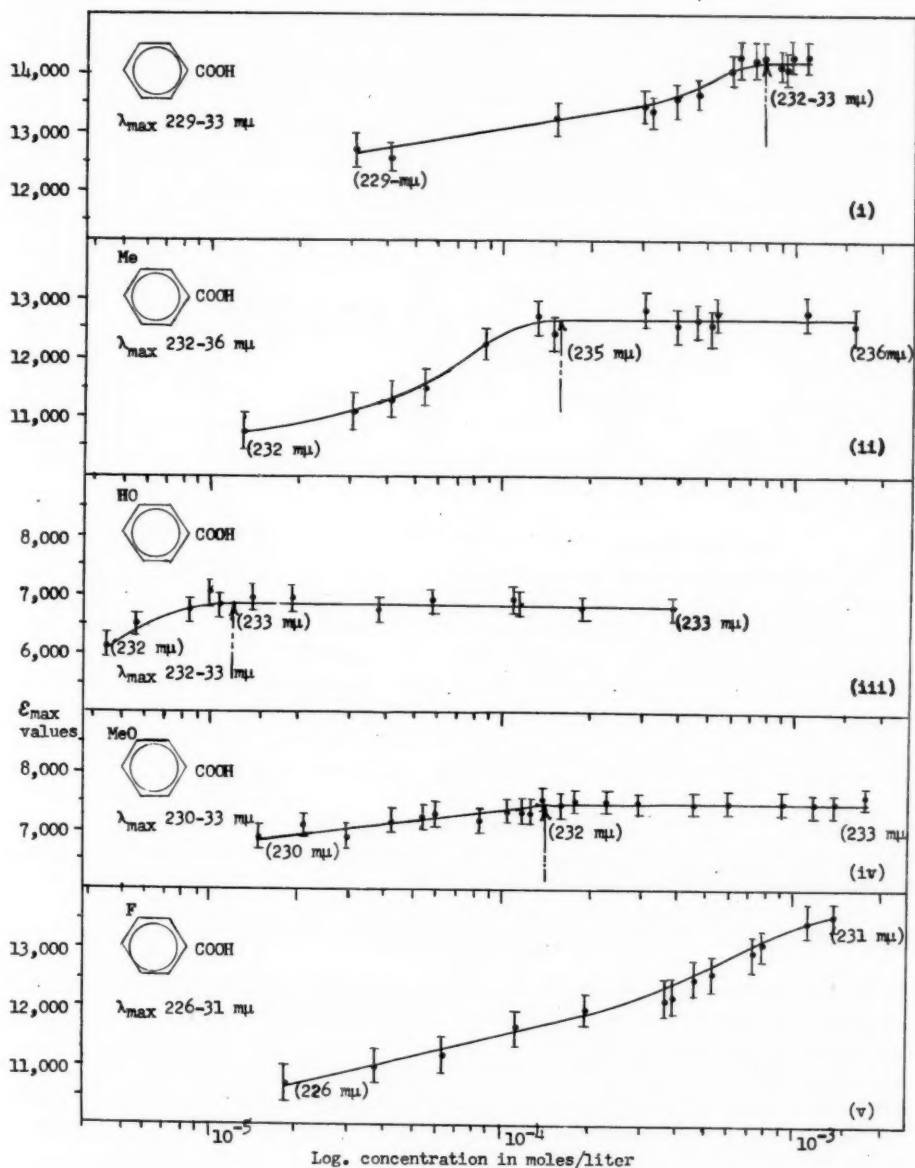


FIG. 3. The variation of  $\epsilon_{\max}$  on changing the solute concentration in cyclohexane solution for (i) benzoic acid, (ii) *m*-toluic acid, (iii) *m*-hydroxybenzoic acid (in cyclohexane solution containing 5% ether), (iv) *m*-methoxybenzoic acid (in cyclohexane solution containing 5% ether), and (v) *m*-fluorobenzoic acid.

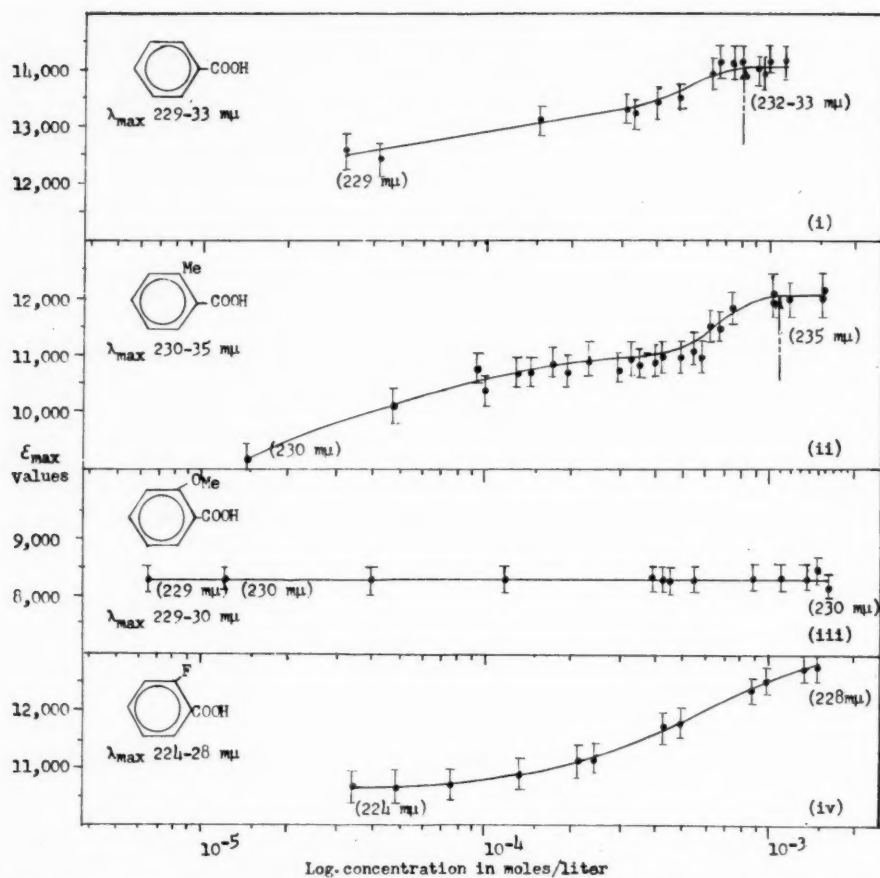


FIG. 4. The variation of  $\epsilon_{\max}$  on changing the solute concentration for (i) benzoic acid, (ii) *o*-toluic acid, (iii) *o*-methoxybenzoic acid, and (iv) *o*-fluorobenzoic acid.

#### THE STRENGTH OF THE DIMERIC HYDROGEN BOND IN SUBSTITUTED BENZOIC ACIDS

The observed spectral changes for a number of substituted benzoic acids on altering the solute concentration are listed in Figs. 1, 3, and 4 and all the available critical maximal concentrations are listed in Table I.

In the absence of a more quantitative interpretation of the underlying effect, which causes the observed concentration dependences, a detailed analysis of the individual compounds in terms of inductive, mesomeric, and steric effects is perhaps not justified at this stage, but the following observations may be made:

(i) The critical maximal concentrations, which represent a qualitative measure of the strength of the dimeric hydrogen bond in substituted benzoic acids, may be compared with the results obtained from other measurements, for example, with the changes in acid strength on introducing a substituent in benzoic acid, with the wavelength displacements

TABLE I  
Critical maximal concentrations (see text) and infrared data for benzoic acids

Substituent	Ultraviolet data, critical maximal concentrations	Infrared data in carbon tetrachloride at a solute concentration of ca. $3.5 \times 10^{-2}$ moles/l.		
		$\nu_{\max}$ values of carbonyl bands		Apparent ratio of intensities, $B_{\text{dimer}}/B_{\text{monomer}}^*$
	Solute concentration in moles/liter $\times 10^4$	$\nu_{\max}$ (dimer), $\text{cm}^{-1}$	$\nu_{\max}$ (monomer), $\text{cm}^{-1}$	
H	8.0†	1696	1744	ca. 10:1
<i>p</i> -CH <sub>3</sub>	4.7†	1695	1739	ca. 10:1
<i>p</i> -OH	0.4†		Insufficiently soluble	
<i>p</i> -OCH <sub>3</sub>	0.34		Insufficiently soluble	
<i>p</i> -F	‡	1697	1744	ca. 10:1
<i>m</i> -CH <sub>3</sub>	1.6	1694	1741	ca. 10:1
<i>m</i> -OCH <sub>3</sub>	1.4	1695	1740	ca. 10:1
<i>m</i> -OH	0.12		Insufficiently soluble	
<i>m</i> -F	‡	1701	1746	ca. 10:1
<i>o</i> -CH <sub>3</sub>	11	1694	1741	ca. 10:1
<i>o</i> -OH	14†	1657	1691	ca. 5:1
<i>o</i> -OCH <sub>3</sub>	‡	1700	1749	ca. 0.9:1
<i>o</i> -F	‡	1704	—	15:1
2,4,6-Tri- <i>t</i> -butyl	‡	1696	1750	ca. 10:1

\* $B$  is the apparent integrated absorption intensity calculated from  $B = 2.93 \times \Delta \nu^2 \times \epsilon^2$ .

†Value from Part II (1).

‡Not within range.

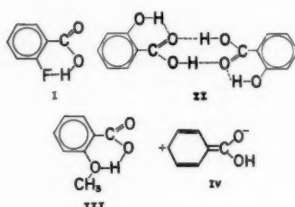
observed in the ultraviolet region, and with the standard heats of dissociation,  $\Delta H$ , of different benzoic acids (cf. refs. 2, 3, 4, 5). These comparisons are found to show general similarities since all the data indicate that a *m*-methyl, *p*-methyl, or *p*-hydroxy substituent in benzoic acid strengthens the dimeric hydrogen bond and that an *o*-methyl, *o*-hydroxy, or *o*-methoxy substituent weakens the dimeric hydrogen bond. Most of the data, though not all, agree in indicating that a *p*-methoxy substituent strengthens the intermolecular hydrogen bond in benzoic acid and that a *m*-fluoro substituent weakens the intermolecular hydrogen bond. The disagreements in the latter two benzoic acids require further investigation.

(ii) Conflicting conclusions are suggested by the data for *p*- and *o*-fluorobenzoic acid. Particularly for *o*-fluorobenzoic acid, the almost complete absence of monomer in the infrared carbonyl absorption (see Fig. 2) suggests that the monomer is destabilized by the *o*-fluoro substituent, and this therefore points against any significant contribution of structures of type I. Other data, however, suggest the presence of such an intramolecular hydrogen bond (cf. ref. 5).

Moreover, the present data also suggest that a *m*-methoxy or a *m*-hydroxy substituent strengthens the intramolecular hydrogen bond in benzoic acid (see Table I and Fig. 3). This is of interest since the ordinary inductive effect of these *m*-substituents, on account of the greater electronegativity of the oxygen atom, would be expected to cause an electron withdrawal from the carboxyl group thus leading to an increase in the proportions both of the ionized acid and the monomeric species. Moreover, the increased acidity is, in fact, observed (4).

(iii) Steric interactions—that is, the loss of resonance energy because of non-planarity—presumably account for the greater critical maximal concentration in *o*-toluic acid (see Fig. 4). Incidentally, there is no evidence, as judged from the intensities of the infrared

carbonyl bands, that steric interactions completely prevent dimer formation, since even for 2,4,6-tri-*t*-butylbenzoic acid at a solute concentration of  $2.5 \times 10^{-2}$  moles/liter the apparent ratio of intensities ( $B_{\text{dimer}}/B_{\text{monomer}}$ ) is still ca. 10:1 (cf. Table I).



(iv) An intramolecular hydrogen bond has previously been postulated to weaken the dimeric hydrogen bond in salicylic acid (I). An intramolecular hydrogen bond in *o*-methoxybenzoic acid may likewise account for the absence of concentration dependence within the investigated concentration range for the solutions of *o*-methoxybenzoic acid (see Fig. 4), if it is assumed that the molecule exists in the monomeric form. The difference between the ultraviolet data in Table I (which indicate that salicylic acid forms a weak dimeric hydrogen bond, whereas *o*-methoxybenzoic acid forms no dimeric bond under identical conditions) and the acid dissociation data (which indicate the opposite tendency in the relative strengths of the intramolecular hydrogen bonds (4)) can be related to the observation that while the intramolecularly hydrogen-bonded form of salicylic acid is still able to form a dimeric hydrogen bond as in II, though not necessarily at the same time, this is not readily possible for the intramolecularly hydrogen-bonded form of *o*-methoxybenzoic acid (III).<sup>\*</sup> A different argument, however, applies to the acid dissociation data, where the intramolecular hydrogen bond in structure II may be assumed to decrease the electron density on the carboxyl oxygen atoms and in this way *increase* the acidity of the carboxyl group; for *o*-methoxybenzoic acid, on the other hand, the *only* intramolecularly hydrogen-bonded form possible (III) tends to retain the active hydrogen atom by means of this hydrogen bond and in this way the acidity may not be increased to nearly the same extent as in salicylic acid (see ref. 4). Further evidence for the presence of a fairly strong intramolecular hydrogen bond in *o*-methoxybenzoic acid is provided by the intensity ratios of the infrared carbonyl bands which clearly indicate the relative predominance of the monomer in *o*-methoxybenzoic acid compared with the much smaller proportion of monomer in other substituted benzoic acids (see Fig. 2 and Table I).<sup>†</sup>

#### ACKNOWLEDGMENTS

The receipt of research grants from the National Research Council of Canada and from the Research Corporation of New York is gratefully acknowledged.

<sup>\*</sup>cf. Reference 5 which also reports considerably more dimeric dissociation for *o*-methoxybenzoic acid than for salicylic acid and see footnote 19 of that paper for a discussion of the structure of *o*-methoxybenzoic acid.

<sup>†</sup>The similarity of the ultraviolet maxima for benzoic acid (monomer) and *o*-methoxybenzoic acid at ca. 230 mμ (see Fig. 4) is also of interest since it suggests that the ultraviolet maxima are not appreciably affected by intramolecular hydrogen bonding of type III, whereas intramolecular hydrogen bonds as shown in II give rise to appreciable bathochromic wavelength displacements (1). This is consistent with the explanation that resonance structures of type IV may be considered to be of predominant importance in determining these wavelength displacements in the ultraviolet region.

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# A STUDY OF THE DIMER OF ETHYLENE PLATINOUS CHLORIDE BY PROTON MAGNETIC RESONANCE<sup>1</sup>

LEONARD W. REEVES

## ABSTRACT

The proton magnetic resonance line of the powdered ethylene platinous chloride dimer complex has a second moment of  $13.68 \pm 1$  gauss<sup>2</sup> at 77° K and an over-all line width of  $11.15 \pm 0.4$  gauss. Measurements at various temperatures between 77° and 329° K show that both second moment and line width decrease slightly with temperature. The mean separation of the doublet observed at 77° K is found to be  $4.80 \pm 0.3$  g.

The results are interpreted in terms of a distorted ethylene molecule whose interproton distances correspond to an intermediate structure between ethylene and an ethane in a *cis* configuration but with two of the *cis* protons removed. This is consistent with earlier studies of the Raman spectrum. The  $\pi$ -type bond formed between a metal *d* orbital and an ethylene  $\pi^*$  orbital is also consistent with the lack of rotation of ethylene at elevated temperatures.

Available results from high-resolution proton resonance studies of ethylene complexed to metal atoms in solutions is discussed.

The bonding of ethylene to the metal in a series of olefin complexes of platinum and palladium II has been treated by Chatt and Duncanson (1). A satisfactory explanation of the infrared and dielectric studies has been achieved in terms of a  $\sigma$  and  $\pi$  bond. The ethylene is co-ordinated to a  $dsp_2$  metal orbital by use of the ethylene  $\pi$  electrons in a  $\sigma$  bond. It has also been suggested that a donation of charge from a metal *d* orbital into the ethylene  $\pi^*$  orbital forms a  $\pi$ -type bond which also contributes to the stability of the complex.

Further studies of these compounds by X-ray diffraction of the solid have confirmed the suggestions of the earlier workers. Studies of Zeise's salt (2), ethylene palladium chloride dimer (3), and styrene palladium chloride (4) show that the ethylene is at one corner of the square planar complex with the metal at the center. Resolution was adequate to show the scattering from the carbon electrons indicating that the carbon atoms are an equal distance above and below the plane of the complex. In the dimers, such as  $[\text{PdCl}_2\text{C}_2\text{H}_4]_2$ , there are two chlorine atoms which act as a bridge between the two palladium atoms; the ethylene in the dimer units complexes in the *trans* positions.

The infrared studies of the C—C stretching mode region indicate the loss of a center of symmetry by the olefin since a weakly allowed infrared absorption occurs in ethylene platinous chloride. The transition moment of this band in the  $1500\text{ cm}^{-1}$  region is very low and it is not observed in Zeise's salt. It is thus evident that the symmetry of ethylene is very little changed by co-ordination. Well-defined C—H stretching frequencies at 3068, 3034, and  $3010\text{ cm}^{-1}$  can be assigned to the three olefin stretching modes in the spectrum of  $\text{K}[\text{C}_3\text{H}_6\text{PtCl}_3] \cdot \text{H}_2\text{O}$ , a propylene complex.

Since the X-ray studies are unable to detect the proton positions and a certain loss of symmetry of ethylene is suggested by infrared measurements, the present study of proton resonance in the powdered solid ethylene platinous chloride is designed to detect any change in the interproton distances of ethylene on co-ordination and confirm the  $\sigma$  and  $\pi$  bonding proposed (1) by showing the absence of rotation of ethylene about the platinum-platinum axis at elevated temperatures.

<sup>1</sup>Manuscript received February 4, 1960.

Contribution from the Department of Chemistry, University of British Columbia, Vancouver 8, British Columbia.

## EXPERIMENTAL

The Varian 40-Mc/s n.m.r. spectrometer V-4250 was used to take spectra at various temperatures from 77° K to 56° C. Spectra at liquid nitrogen temperature were measured using a Dewar which was mounted in a threaded cylinder replacing the Varian high-resolution spinner turbine housing on the induction probe. This was machined inside to fit a standard ground-glass joint. The small half-silvered Dewar was made with a standard taper joint on the outside and during the experiment the Dewar was located in the aluminum cylinder so that the Dewar was just fitted into the 15-mm 40-Mc/s Varian insert and was clear of the bottom of the insert by 1 mm. By careful machining of the locating cylinder actual contact of the insert with the Dewar was avoided so that changes in probe balance due to vibration and movement of the whole probe could be prevented. By thinning out the glass walls of an 8-mm sample tube a favorable proton-packing factor could be achieved. The liquid nitrogen was filtered through glass wool to prevent ice passing into the the Dewar. The Dewar contained enough liquid nitrogen to allow one spectrum to be taken without refilling. Exact reproduction of spectra was obtained. Above -30° C spectra were obtained by use of a second apparatus which will be described in a forthcoming paper by Reid and Connor (7), or with an apparatus described by Bernstein, Schneider, and Pople (7).

The main magnetic field was modulated at 80 c.p.s. and swept across resonance at calibrated rates. Calibration was achieved by observing the signal from liquid water with a modulation width of 30 milligauss and superimposing 5-, 10-, or 20-kilocycle side bands from a Hewlett-Packard audio oscillator, which was, in turn, calibrated against a Hewlett-Packard Model 5243 electronic counter. The recorder chart paper could thus be calibrated in gauss per centimeter before and after each series of experiments. No variation in calibration of sweep rates at a given setting was observed throughout the whole series of experiments.

The ethylene platinumous chloride showed 98% purity in ethylene content as determined by comparison of the intensity of the high-resolution proton resonance in standard acetonitrile solutions with standard solutions of ethylene gas in the same solvent. The compound was prepared in the laboratory of Professor Orchin at the University of Cincinnati and kindly supplied by courtesy of the Gulf Oil Multiple Fellowship at the Mellon Institute.

## RESULTS

Preliminary experiments showed that except at very low r.f. power there was some saturation of the proton resonance. The low power required to avoid signal distortion due to saturation was not practicable for good quantitative measurement of the resonance line parameters. A short irradiation of  $\frac{1}{2}$  hour with 50-kv X rays produced sufficient paramagnetic impurity to allow the use of much higher r.f. power giving a signal-to-noise ratio of approximately 30 to 1, with modulation widths of 1 gauss. The paramagnetic impurities persisted at the highest temperature 56° C. There was no systematic difference in line width parameters calculated from the experiments with low r.f. power and those with higher r.f. power with irradiated samples. Thus the impurities introduced by X irradiation did not reach a concentration at which broadening of resonance lines occurs because of large local fields due to the electronic paramagnetism of the impurities (8).

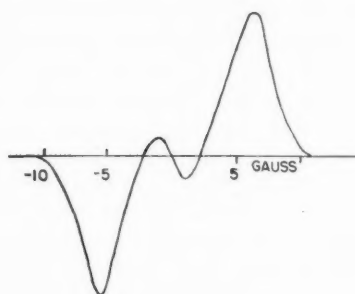


FIG. 1. Proton resonance in powdered ethylene platinumous chloride dimer at 77° K.

Figure 1 shows the spectrum of solid ethylene platinumous chloride at liquid nitrogen temperature. The curve represents the derivative of the resonance absorption curve obtained by modulating the large magnetic field  $H_2$  and detecting the slope of the absorption curve over the modulation width with a phase-sensitive detector. The curve shown is the average of five spectra with a signal-to-noise ratio of 30 to 1. The derivative curve shows a clear doublet structure for the absorption as would be expected for the ethylene molecule where two closely spaced protons occur (9). The separation of the two peaks in the absorption curve determined from the average of five spectra at 77° K is  $4.78 \pm 0.3$  gauss. The over-all line width determined from the separation of the positions of maximum and minimum slope in the derivative curve is  $11.15 \pm 0.4$  gauss.

A spectrum at +56° C is shown in Fig. 2. Above -30° C the doublet structure of the

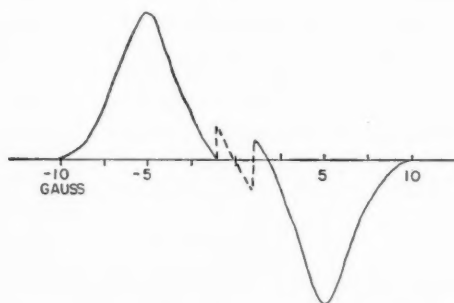


FIG. 2. Proton resonance in powdered ethylene platinumous chloride dimer at 329.7° K.

derivative curve is marred by the appearance of a small impurity peak at the resonance center of modulation width preventing an estimation of the doublet separation. It is possible that this impurity may be traces of solvent used in the preparation or a certain amount of free ethylene with considerable motion in the solid lattice at -30° C.

The second moments obtained are quoted in Table I at all temperatures studied. In each case they are the average values taken for at least three curves. They were computed using the formulas given by Andrew (10).

TABLE I  
Line width and second moments of powdered ethylene  
platinous chloride

Temp., °K	$\Delta(H)$ , line width, gauss	$(\Delta H)^2$ second moment, gauss <sup>2</sup>
77	11.15 $\pm$ 0.4	13.68 $\pm$ 1.0
248	10.00	10.6
267	10.10	10.5
301	10.00	10.6
313	10.17	11.1
320	10.33	10.9
329	10.32	11.2

NOTE: Line widths varied for a given temperature up to 0.4 gauss from the mean; second moments deviated up to 1 gauss<sup>2</sup> from the mean.

The narrow component of modulation width shown in Fig. 2 did not grow in intensity with increasing temperature.

#### DISCUSSION

The Lewis acid-base reaction involving  $\pi$  electrons in olefinic systems and metal ions such as silver, or the halogen molecules, has been studied extensively in optical spectroscopy by observation of the familiar charge transfer bands (11). In the silver-olefin systems an interaction is detected in the Raman spectrum of the olefin by observation of the frequency shift of the C=C stretch (12). This frequency shift in the platinum olefin complexes is about twice that in the silver-olefin association (1).

The chemical shift of the protons from nuclear resonance signals detected in solutions of silver perchlorate in benzene or olefins is almost identical with the proton resonance position in pure benzene or olefin (13). This result is not surprising in view of the fact that  $\pi$  electron density influences the nuclear shielding parameter of a proton directly attached to the olefinic carbon only to a minor extent providing the lifetime of the complex in solution is very short (14). Larger changes in the chemical shift of ring protons in aromatic systems due to complex formation can be ascribed to a specific interaction of a solvent molecule with this proton rather than with  $\pi$  electrons. Large changes in proton chemical shifts (2-5 p.p.m.) in olefins complexed to metal atoms have been observed by Green, Pratt, and Wilkinson (15) and by Lauterbur and Reeves (16). It is expected (15) that such changes in chemical shift in strongly complexed ethylene is due to diamagnetic anisotropy introduced by bonds in the rest of the platinum complex or introduced by  $\sigma$  bond formation using  $\pi$  electrons from the olefin. The bond energy in the platinum-olefin complex is certainly greater than in silver-olefin complexes so that it is possible for chemical exchange effects to minimize chemical shift changes due to diamagnetic anisotropy of an individual complex in the latter case. Further results will be reported in conjunction with Lauterbur at a later date on studies using high-resolution n.m.r.

The suggestions of Chatt and Duncanson (1) are in general confirmed by high resolution studies of proton resonance in solution but these are limited in scope when effects of chemical exchange are not properly taken into account (12). The study of solid complexes using proton resonance will show changes in interproton distances after complex formation (10). The second moment of the resonance absorption line is related to the internuclear distances by the following equation:

$$[1] \quad S = \frac{6}{5} \cdot I(I+1)g^2\mu_0^2N^{-1} \sum_{j>k} r_{jk}^{-6} + \frac{4}{15} \mu_0^2N^{-1} \sum_{j,f} I_f(I_f+1) \cdot g_f^2 \cdot r_{j,f}^{-6}$$

$S$  = second moment of absorption line,

$I$  = nuclear spin quantum number of the proton (nucleus under study),

$g$  = nuclear "g" factor for the protons,

$\mu_0$  = nuclear magneton,

$N$  = number of protons in the system,

$r_{jk}$  = internuclear distance between nuclei  $j$  and  $k$  in the system,

$g_f$  = nuclear  $g$  factor of nuclear species  $f$  in the system,

$I_f$  = nuclear spin quantum number of nuclear species  $f$ ,

$r_{jf}$  = internuclear distance between proton  $j$  and a nucleus  $f$  of the  $f$  system.

The second moment of an isolated ethylene molecule is calculated to be 11.05 gauss<sup>2</sup>. A theoretical second moment for an undistorted ethylene molecule, complexed in the platinum ethylene chloride dimer, can be estimated using the crystal structure of the ethylene palladium chloride dimer since the atomic radius of palladium is very little different from platinum (3). The proton nuclear moment system gives rise to a second moment contribution almost equal to that in the isolated ethylene molecule. The closest approach of a proton outside the ethylene molecule in the crystal is 4.67 Å. The contribution of protons in the crystal outside the ethylene molecule can be obtained by replacing the first summation in equation 1 by an integral between 4.67 Å and infinity (18). The volume of unit cell is 1038 Å<sup>3</sup> and this contains four dimers or 16 protons or  $1.54 \times 10^{-2}$  protons per cubic Å

$$[2] \quad S_{\text{inter}} = \frac{4 \cdot \pi \cdot 357 \cdot 8 \cdot \rho}{3} \left( \frac{1}{r^3} \right)_{\infty}^{4.47}$$

The first summation replaced by an integral is given by equation 2, where 357.8 corresponds to the presummation term evaluated for  $r$  expressed in Å,  $\rho$  is the density of protons per cubic Å. Sinter (evaluated between 4.67 Å and  $\infty$ ) gives a value 0.22 gauss<sup>2</sup>. There will be small contributions from the 33.7% Pt<sup>195</sup> and Cl<sup>35</sup> and Cl<sup>37</sup>; these will only be effective within the same dimer. The platinum nuclear moment contributes only  $5 \times 10^{-3}$  gauss<sup>2</sup> and this has been neglected. The chlorine contributions are approximately  $1 \times 10^{-2}$  gauss<sup>2</sup> and can also be neglected in the second moment.

The theoretical second moment for the proton resonance line in ethylene platinous chloride is therefore 11.3 gauss<sup>2</sup>. This is considerably less than the measured value and the discrepancy can only be due to a modification of the interproton distances in the ethylene molecule.

The modification of distances is expected to involve a lengthening of the C—C bond due to lowering of bond order since some  $\pi$  electron density is located between the C—C axis and the platinum atom in the  $\sigma$  bond. The C—H bond distances would not be expected to change greatly but the complexing will cause this C—H bond to lean back from the direction of the platinum atom. In fact the general structure of the ethylene in the complex will approach that of ethane with one hydrogen missing on each carbon.

The second moment calculated from such a hypothetical arrangement in the crystal of ethylene platinous chloride would be 14.75 gauss<sup>2</sup>. The experimental second moment of 13.68 gauss<sup>2</sup> has an intermediate value between the undistorted ethylene and ethane structures. Since the lowering of bond order in the C—C bond tends to lower the

theoretical moment and the leaning back of the C—H bonds tends to raise it, then it is possible to fit the experimental second moment with a wide range of C—C distances and H—C—H angles. It is evident, however, that the distortion of ethylene suggested by Chatt and Duncanson (1) is consistent with the present study.

The n.m.r. spectrum of a rigid closely spaced proton pair in a polycrystalline material is a doublet provided all other interacting protons are sufficiently distant. The separation of the doublet is related to the proton separation in the pair by (10)

$$[3] \quad \frac{3\mu}{r^3} \cong \Delta H_{\text{doublet}}$$

This separation is a minimum value of the splitting since the system consists of nuclei outside the closely interacting and this causes broadening of the doublet and a reduction of the splitting. Equation 3 gives a value of  $r = 2.08 \text{ \AA}$  in this case. The separation of 1.1 protons in pure ethylene is  $1.85 \text{ \AA}$  and in ethane  $1.78 \text{ \AA}$ . The precision of the present result is particularly limited since the distance between cis protons in ethylene is  $2.42 \text{ \AA}$ . The cis proton-proton distance invalidates the 'interacting pair' assumption and causes the observed doublet structure to correspond to proton separations between  $1.85$  and  $2.42 \text{ \AA}$ . The second moments observed and calculated in this work are consistent with the results obtained previously from Raman spectra of this compound in solution (1).

If the ethylene were not located by  $\pi^*$  bonds it is likely that rotation about an axis perpendicular to the C—C axis would occur. This is not observed. The small decrease in second moment between  $77^\circ \text{ K}$  and  $329^\circ \text{ K}$  can be accounted for on the basis of rocking motions perpendicular to platinum-ethylene bond and on wagging about the C—C axis. This is a good evidence therefore for the additional  $\pi^*$  attachment suggested.

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## NOTES

### HEAT OF MIXING OF CARBON TETRACHLORIDE WITH FURFURAL

S. K. JEUN AND BENJAMIN C.-Y. LU

In the course of investigations of various thermodynamic properties of solutions, the heat of mixing of carbon tetrachloride and furfural over the complete concentration range was determined at 27° and 40° C in a Dewar calorimeter of a type similar to that used by Tsao and Smith (1) and Murti and van Winkle (2). Heating and cooling curves were taken before and after mixing for each determination and were used to eliminate the possible errors due to radiation, vaporization, and condensation, following a procedure which modified that proposed by Williams (3) for determining specific heats of liquids.

The heat-of-mixing data are expressed in terms of the amount of heat absorbed per mole of mixture when the pure components are mixed at constant temperature and pressure. The results are listed in Table I and are represented in functions of the mole

TABLE I  
Experimental data

System carbon tetrachloride - furfural at 27° C		System carbon tetrachloride - furfural at 40° C	
Mole fraction furfural	Heat of mixing, cal/mole mixture	Mole fraction furfural	Heat of mixing, cal/mole mixture
0.041	68.1	0.021	37.5
0.120	157.2	0.048	76.3
0.231	216.6	0.064	97.2
0.355	241.0	0.094	134.6
0.453	234.3	0.108	146.2
0.563	210.7	0.171	206.3
0.684	167.1	0.265	260.7
0.792	117.2	0.307	289.8
0.903	58.0	0.437	298.1
		0.547	281.2
		0.658	244.9
		0.746	182.2
		0.778	166.3
		0.816	135.3
		0.820	141.0
		0.865	102.4
		0.875	95.4
		0.917	65.4
		0.923	56.8
		0.951	38.2
		0.967	25.0

fraction of furfural by Fig. 1. The maximum error resulting from vaporization and condensation effects and in the measurement of experimental data was estimated to be 2%. Repeated runs at fixed condition indicated that the data were reproducible with a discrepancy of less than 1%. It is believed that the results presented have an accuracy of 2% or better.

It is observed that the heat of mixing data are positive over the temperature range investigated. The temperature effect on heat of mixing in the diluted furfural solutions seems to be negligible, while in the concentrate furfural solutions the heat of mixing is increased by increasing the temperature. It may be concluded that over the temperature range investigated the logarithm of the activity coefficient of furfural at infinite dilution

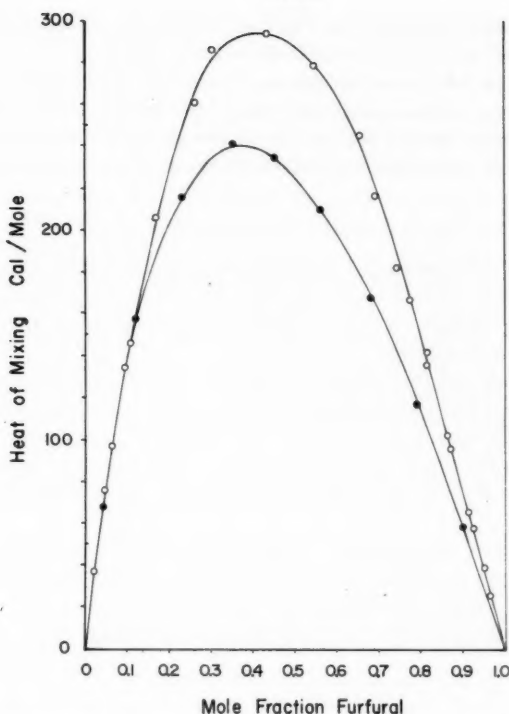


FIG. 1. Heat of mixing data for system carbon tetrachloride-furfural. ● 27° C, ○ 40° C.

varies linearly with the reciprocal of the absolute temperature and that the temperature effect on the activity coefficient of carbon tetrachloride at infinite dilution is more complex.

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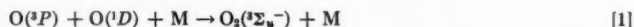
#### A POSSIBLE MECHANISM FOR THE PRODUCTION OF $O_2^*(^3\Sigma_u^-)$ IN FLAMES

ROBERT J. FALLON, IRWIN TOBIAS, JOSEPH T. VANDERSLICE, AND WILLIAM G. MAISCH

The emission spectra of a number of flames containing oxygen show the Schumann-Runge (1-6) bands which are associated with the transition  $B^3\Sigma_u^- \rightarrow X^3\Sigma_g^-$  in  $O_2$ . The mechanism for the production of  $O_2^*(^3\Sigma_u^-)$  in flames has been a matter of concern for some time (4-6). Originally, it was suggested that it might be produced through a chemical reaction (7), and both Laidler (7) and Shuler (8) have suggested possible reactions which might account for the presence of these bands in various flames. It is now felt, however,

that the  $O_2^*(^3\Sigma_u^-)$  is formed thermally and not as a result of any chemical process (5, 9).

Laidler (4) has pointed out that, although the mode of formation of  $O_2^*(^3\Sigma_u^-)$  might be specific for each flame, the fact that this species occurs in so many different flames would seem to indicate that the reactions leading to the production of  $O_2^*(^3\Sigma_u^-)$  are common to all flames and thus independent of the nature of the fuel. He has suggested, therefore, that the reaction initially proposed by Feast (10) to explain the production in a high pressure arc



must be considered as a possible source of the excited  $O_2$  molecule since atomic oxygen is definitely present in  $H_2/O_2$  and  $CO/O_2$  flames (11). The  $O(^1D)$  may be produced thermally since its excitation energy is only 1.97 eV or it may be produced by the thermal dissociation of one of the reaction intermediates.

There are several difficulties in considering reaction [1]. No evidence for excited atomic oxygen has been found in the  $CO/O_2$  flame (1). Also, if reaction [1] were responsible for the production of the Schumann-Runge bands, one might expect that transitions involving some of the higher vibrational levels of the  $B^3\Sigma_u^-$  state would be observed. However, only the lower vibrational levels ( $v' = 0, 1, 2$ ) have been seen in the  $CO/O_2$  and  $H_2/O_2$  flames (1, 6).

The purpose of this note is to suggest a mechanism for the production of thermally excited  $O_2^*(^3\Sigma_u^-)$  in flames on the basis of some recently determined potential curves of  $O_2$  (12). The methods of obtaining these curves are discussed in reference (12) and those of importance in the present discussion are shown in Fig. 1. It is found that the  $^3\Pi_u$  and

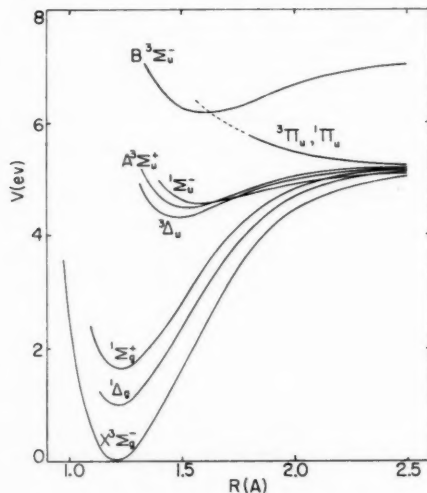
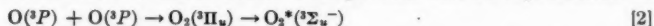


FIG. 1. Potential energy curves for  $O_2$ .

the  $^1\Pi_u$  have approximately the same energy of interaction and seem to cross the curve for the  $B^3\Sigma_u^-$  state around the minimum. Of all the repulsive states which arise from the interaction of two ground-state atoms, only the  $^3\Pi_u$  can predissociate the  $B^3\Sigma_u^-$  state strongly according to Kronig's rules (13). An oxygen molecule in the  $^3\Pi_u$  state can, there-

fore, make a non-radiative transition to the  $B$  state. This process can be represented as



and requires an energy of only about 1 ev. An excitation process like [2] would explain why the observed Schumann-Runge bands originate only from the lower vibrational levels of the  $B$  state. One might also expect that the rate of reaction [2] is much greater than that of [1] since the latter is a three-body collision.

If the above mechanism is correct, then it would be of interest to speculate on possible processes that might contribute to the continuum that has been noticed in some flames (14). In the  $H_2/O_2$  and  $NH_3/O_2$  flat diffusion flames, a continuum has been observed that lies roughly in the same region as the Schumann-Runge emission. Since this is near the oxygen side of the flame, Gaydon (14) suggests atomic oxygen as one of the reactants. Radiative transitions from the  $^3\Pi_u$  or  $^1\Pi_u$  state to some of the lower attractive states would result in a continuum. One would expect this continuum to arise from the same region of the flame as the Schumann-Runge bands in agreement with the observations. There are other transitions that could contribute to the continuum, for example, a transition from the repulsive side of the  $A^3\Sigma_u^+$  state to the ground state. One might expect, however, that these would not be strong since they are not permitted by the selection rules although the latter might well be relaxed at these pressures.

A continuum has also been observed in flames containing carbon monoxide (15). This has been studied recently by Kaskan (16), who concludes that the production reaction involves an oxygen atom and a carbon monoxide molecule. However, since the Schumann-Runge bands are observed in these flames (15) there is a possibility that a small amount of the continuum might be due to the interaction of two oxygen atoms as suggested by Hoare and Walsh (17) and Hornbeck (18).

In conclusion, we would like to suggest that the  $O_2(^3\Sigma_u^-)$  found in flames burning with  $O_2$  is formed by the thermal collision of two  $O(^3P)$  atoms interacting along the  $^3\Pi_u$  repulsive curve which undergoes a radiationless transition to the  $^3\Sigma_u^-$  state. Also, part of the continuum observed in these flames might arise from transitions from the repulsive branches of the  $A^3\Sigma_u^+$ ,  $^3\Delta_u$ , or  $^1\Sigma_u^-$  states down to one of the lower attractive states.

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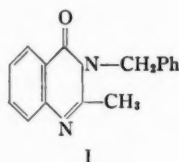
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## 3-BENZYL-2-METHYL-3,4-DIHYDRO-4-KETOQUINAZOLINE

RAGINI ANET\* AND S. SOMASEKHARA

As a part of investigations (1) on fused heterocyclic systems incorporating the quinazoline nucleus, 3-benzyl-2-methyl-3,4-dihydro-4-ketoquinazoline (I) was required. A preparation of this base was reported by Bogert and Beal (2) from acetylanthranil and benzylamine. However, these workers analyzed their compound, m.p. 123°, for nitrogen only, and did not prepare any derivatives. A hydrochloride, m.p. 232°–234°, of the required base was prepared by Grimm, Guenther, and Morgan (3) from acetylanthranilic acid and benzylamine in presence of phosphorus trichloride. Once again, the compound was poorly characterized, no analysis figures were reported, nor was the free base or any derivatives prepared. As 2-methyl-4-hydroxy-quinazoline (II) was readily available, we studied its alkylation with benzyl chloride.



Treatment of the potassium salt of II with benzyl chloride in acetone gave a product whose analysis and infrared spectrum (4) were consistent with structure I. The melting point (74°) was different from that reported by Bogert and Beal, although that of the hydrochloride of our base was in agreement with that reported by Grimm *et al.* The alkylation of 4-hydroxyquinazolines with alkyl halides in presence of alkali normally gives the 3-alkyl derivatives but in view of the reported ethylation of the sodium salt of 4-hydroxyquinazoline with ethyl iodide in alcohol to give largely the 4-ethoxy derivatives (5), an alternate synthesis of I was carried out from *o*-nitrobenzoyl chloride via N-benzyl-*o*-nitrobenzamide, N-benzyl-*o*-aminobenzamide, and N-benzyl-*o*-acetylaminobenzamide (III). The quinazoline derivative obtained by the cyclization of III with aqueous benzylamine was identical (mixed melting points and infrared spectra) with our benzylation product.

Having established that the product obtained on benzylation of II was indeed the required base I, it was of interest to find out the nature of Bogert and Beal's compound. Repetition of their work gave at first a product identical with our benzylation product. However, if slightly less than the calculated amount of benzylamine was used, a compound, m.p. 118°, could be obtained. Its infrared spectrum showed all the bands present in the spectrum of I but in addition showed bands in the —NH or —OH stretching region similar to those shown by the spectrum of N-benzyl-*o*-acetylaminobenzamide III. In fact, the compound was an equimolecular complex of I and III. This was shown by its elementary analysis and by its separation with cold dioxane into the two components. Oxidation of I with selenium dioxide in aqueous dioxane gave the 2-aldehyde, which was characterized as its 2,4-dinitrophenylhydrazone.

It is of interest to note that the hydrochloride of I underwent debenylation at its melting point.

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## EXPERIMENTAL

*3-Benzyl-2-methyl-3,4-dihydro-4-ketoquinazoline (I)*

2-Methyl-3,4-dihydro-4-ketoquinazoline (8.5 g), benzyl chloride (7 g), and powdered potassium hydroxide (12 g) were refluxed in 500 ml of acetone for 6 hours. After removal of the solvent, the residue was extracted with chloroform and the chloroform evaporated. The oil thus obtained was treated with cold dilute hydrochloric acid to give a crystalline hydrochloride. Liberation of the base in the usual manner gave 5 g of the 3-benzyl derivative (I), which was crystallized from benzene - petrol ether (30°-60° b.p.) in plates, m.p. 74°. Found: C, 76.6; H, 5.5; N, 11.0%. Calc. for  $C_{16}H_{14}NO_2$ : C, 76.8; H, 5.6; N, 11.2%.

The hydrochloride, prepared by cooling a hot solution of the base in hydrochloric acid, formed needles, m.p. 233° (lit. (2), m.p. 232°-234°). Found: N, 9.2%. Calc. for  $C_{16}H_{16}N_2OCl \cdot H_2O$ : N, 9.2%.

Acetylanthranyl (0.9 g) and benzylamine (0.6 g) were heated together at 150° for 30 minutes. On cooling, the melt solidified and was treated with aqueous sodium bicarbonate to give 0.9 g of a white solid. After several crystallizations from ethanol it melted at 118°. (Bogert and Beal (2) give m.p. 123°.) Found: C, 74.0; H, 5.9; N, 10.8%. Calc. for  $C_{16}H_{14}N_2O \cdot C_{16}H_{16}N_2O_2$ : C, 74.1; H, 5.8; N, 10.8%.

The compound was soluble in hot benzene, alcohol, and chloroform. Treatment with a small quantity of cold benzene gave a benzene-soluble compound, m.p. 74°, identical with I and a residue, m.p. 129°-137°, which after crystallization from aqueous alcohol melted at 147° to 148°, identical with N-benzyl-*o*-acetylaminobenzamide (IV) described below.

Repetition of the above experiment with a slight excess of benzylamine gave I exclusively.

*3-Benzyl-3,4-dihydro-4-ketoquinazoline-2-aldehyde*

Freshly prepared selenium dioxide (0.42 g) was added to 1 g of I in 25 ml dioxan and the mixture was refluxed for 1 hour. The precipitated selenium was filtered off and the filtrate passed through a 3-in. column of alumina to remove colloidal selenium. The dioxan solution was concentrated and the residue treated with petrol ether to give 1 g of the aldehyde, which crystallized from benzene in needles, m.p. 143°-144°. Found: C, 72.4; H, 4.6; N, 10.7%. Calc. for  $C_{16}H_{12}O_2N_2$ : C, 72.7; H, 4.5; N, 10.6%.

The 2,4-dinitrophenylhydrazone prepared in the usual manner, gave needles, m.p. 275°-277°. Found: N, 19.1%. Calc. for  $C_{22}H_{16}N_6O_8$ : N, 18.9%.

*N-Benzyl-*o*-nitrobenzamide*

*o*-Nitrobenzoic acid (1 g) and thionyl chloride (3 ml) were refluxed in 5 ml of dry benzene for 1 hour. The solution was concentrated under reduced pressure and the residue was dissolved in 2 ml of dry benzene. To a cold solution of the acid chloride, a solution of 1 ml benzylamine in 3 ml benzene was added, followed by 10 ml of petrol ether. The crude benzamide (1.1 g), m.p. 122°-123°, separated out and was crystallized from benzene. Found: N, 10.9%. Calc. for  $C_{14}H_{12}O_3N_2$ : N, 10.9%.

*N-Benzyl-*o*-aminobenzamide*

A 1-g quantity of the *o*-nitrobenzamide was gently refluxed with 3 g of zinc dust in 100 ml of 5% acetic acid for 2 hours, and filtered hot. The filtrate, on cooling, gave the *o*-amino derivative, m.p. 123°. It was crystallized from aqueous alcohol in needles, m.p. 124°. Found: N, 12.6%. Calc. for  $C_{14}H_{14}ON_2$ : N, 12.4%.



*N-Benzyl-o-acetylaminobenzamide* (III)

One hundred milligrams of the *o*-amino derivative was heated with 3 ml of acetic anhydride at 100° for 10 minutes. The reaction mixture was cooled and poured into water to give 100 mg of the acetyl derivative. It was crystallized from aqueous alcohol in needles, m.p. 147°–148°. Found: C, 71.4; H, 5.9; N, 10.5%. Calc. for  $C_{16}H_{16}N_2O_2$ : C, 71.6; H, 6.0; N, 10.5%.

*Cyclization of the N-Benzyl-o-acetylaminobenzamide*

Fifty milligrams of the acetylmino derivative was added to 3 ml of water containing two drops of benzylamine. The mixture was boiled for 2 to 3 minutes and cooled. Dilute hydrochloric acid precipitated the hydrochloride (40 mg), which was converted to the base with potassium hydroxide. Chloroform extraction gave an oil which crystallized from benzene – petrol ether in plates, m.p. 73°–74° (mixed m.p. with I, 73°–74°).

*Debenzylation of the Hydrochloride of I*

The hydrochloride of I (0.8 g) was maintained at 235° for 30 minutes. The product was washed with a 5% sodium carbonate solution. Crystallization of the solid from dilute ethanol (charcoal) gave 0.15 g of 2-methyl-4-hydroxyquinazoline (II), m.p. 234° (5). Mixed melting point with an authentic sample was undepressed.

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# NUCLEAR SHIELDING PARAMETERS FOR PROTONS IN STRONG HYDROGEN BONDS I. ORTHOHYDROXY AZO COMPOUNDS

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## INTRODUCTION

In connection with studies of nuclear shielding parameters in strong hydrogen bonds (1, 2) measurements have been made on a series of compounds of the basic skeleton shown below:



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The substituents introduced into the aromatic ring systems will be identified by skeleton type I or II and substitution position related to above numbering system. The correlation of hydrogen bonding strength with nuclear shielding parameter ( $\sigma_{\text{reference}} - \sigma_{\text{OH}}$ ) is now well established (3) although quantitative comparison of ( $\sigma_{\text{ref}} - \sigma_{\text{OH}}$ ) and heat of formation directly is rarely possible. Spectral shifts in the infrared are more often used as the correlative parameter (3, 4). There is an advantage in measuring the shielding parameter in intramolecular hydrogen bonds since in dilute solution the entropy term due to dilution is not dominant in causing dissociation of the bond. This is shown clearly in many dilution shift studies (5, 9, 10) where intramolecular hydrogen bonds exist. If the intramolecular hydrogen bond is fairly weak as in O-chloro phenol, competition with stronger intermolecular hydrogen bonds in concentrated solutions causes dilution chemical shifts in this region. However, even in this case isolation of the hydrogen-bonding species in an inert solvent such as  $\text{CCl}_4$  enables a nuclear shielding parameter for an undissociated intramolecular hydrogen bond to be obtained (5). Changes in nuclear shielding due to hydrogen bonding has been treated theoretically by Marshall and Pople (11).

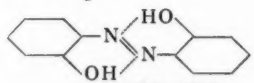
## EXPERIMENTAL

Measurements were made using a solvent 99.5 mole %  $\text{CCl}_4$  and 0.5 mole % cyclohexane in which the compounds were soluble up to 1 mole %, except for nitro derivatives. A 40-Mc/s Varian spectrometer V4300 with field stabilizer VK3506 was used and samples were made up in 5-mm O.D. tubes. The 0.5% cyclohexane served as an internal reference. Chemical shifts were measured by the usual side band technique with an audio oscillator calibrated by using 'lissajoux' figures at multiples of the 60 c.p.s. mains frequency.

## RESULTS AND DISCUSSION

Column 2 of the Table I shows the value of ( $\sigma_{\text{cyclohexane}} - \sigma_{\text{OH}}$ ) measured directly in the manner described. In an attempt to correct for the difference in shielding effect at the proton under study due to the additional diamagnetic anisotropy introduced by the naphthalene rings, a correction has been made to all compounds for the low field shift

TABLE I

Compound	( $\sigma_{\text{C}_6\text{H}_{12}} - \sigma_{\text{OH}}$ ) p.p.m.	( $\sigma_{\text{C}_6\text{H}_{12}} - \sigma_{\text{OH}}$ ) p.p.m. corrected	Compound
I	-11.03	-9.98	1
			
I 3,9-Dimethyl	-10.52	-9.48	2
I 3-Methyl	-11.00	-9.95	3
I 5 —CH= replaces —N=	-10.95	-9.90	4
I 5 —CH= replaces —N=	-11.40	-10.37	5
II	-14.26	-13.06	6
II 9-Methyl	-14.62	-13.42	7
II 11-Methyl	-14.12	-13.92	8
II 9-Chloro	-14.25	-13.05	9
II 11-Chloro	-13.97	-12.77	10

due to currents in all aromatic rings. The correction to high field is slightly larger for the naphthalene compounds. The free electron model of Pople was used (6) and the interatomic distances were those for trans azo benzene (7). In addition the C—O—H bond, lengths and angles were taken to be the same as those in a phenol. The molecule is probably

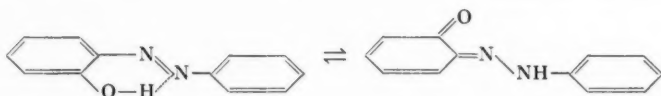
very nearly planar and was taken to be so in the calculation. Column 3 in the table contains shielding parameters corrected in this manner. These values are more correct when comparing with shielding parameters of strong hydrogen bonds in systems without large magnetically anisotropic centers.

The main feature of the results is the large shift of  $\sim 3$  p.p.m. to low field in the naphthalene derivatives indicating a much stronger hydrogen bond. A good measure of the decreased shielding is shown in compounds 1 and 6 which differ by 3.08 p.p.m. It is clear that the electron-withdrawing action of the larger resonance system in naphthalene makes the hydroxyl group a much stronger acceptor. A parallel can be drawn in the greater acidity of the  $\beta$  hydroxy naphthalene over that of phenol (8).

Among the trans azo benzene derivatives the dihydroxy compound 2 has greatest shielding and is thus the weakest hydrogen bond of this series. It is expected that the donor properties of one nitrogen will be affected to a small degree by the use of the other in a hydrogen bond. Methyl substitution is not effective in changing the hydrogen bond strength; however the replacement of one nitrogen by a  $-\text{CH}=\text{N}-$  group leads to decreased shielding of the hydrogen-bonding proton. The difference in electronegativity of nitrogen and the  $-\text{CH}=\text{N}-$  group will increase the donor property of the nitrogen and thus to a small degree the hydrogen bond formed will be stronger.

In the  $\beta$  OH naphthalene derivatives substitution on the benzene ring only was studied. Chlorine substitution has very little effect on chemical shift but the inductive effect of methyl substitution appears to increase donor properties of the conjugated nitrogen considerably, resulting in a stronger hydrogen bond.

Some of these compounds were studied in the melt at higher temperature. In all cases the OH peak showed broadening indicative of proton exchange. The signals in 1%  $\text{CCl}_4$  solution were quite sharp. As the temperature was further raised some OH peaks broadened below noise level (over 40 c.p.s. half width). This proton transfer process may be intermolecular or involve transfer across the intramolecular hydrogen bond. In the latter case the imino form of these compounds would appear in equilibrium with the azo form.



It is of some interest that the imino form has been shown to exist in the solid state in these compounds (12, 13) and the existence in solution is also suggested. Other workers (14) have shown, however, that the azo form of *o*-azophenols is the only stable species in solution. Since it is unlikely that proton transfer to the imino form occurs in dilute  $\text{CCl}_4$  solution at room temperature where the proton resonance of the  $-\text{OH}$  proton is sharp, then the nuclear shielding parameters are attributed to pure azo form. Measurements of the intensity of the methyl resonance in methyl derivatives compared with the intensity of the  $-\text{OH}$  peak showed that no appreciable amount of material is in the imino form. It is presumed that protons transferred to the imino form will not show resonance peaks because of quadrupole relaxation. Intensity measurements in dilute solution cannot be better than  $\pm 5\%$  in this experiment.

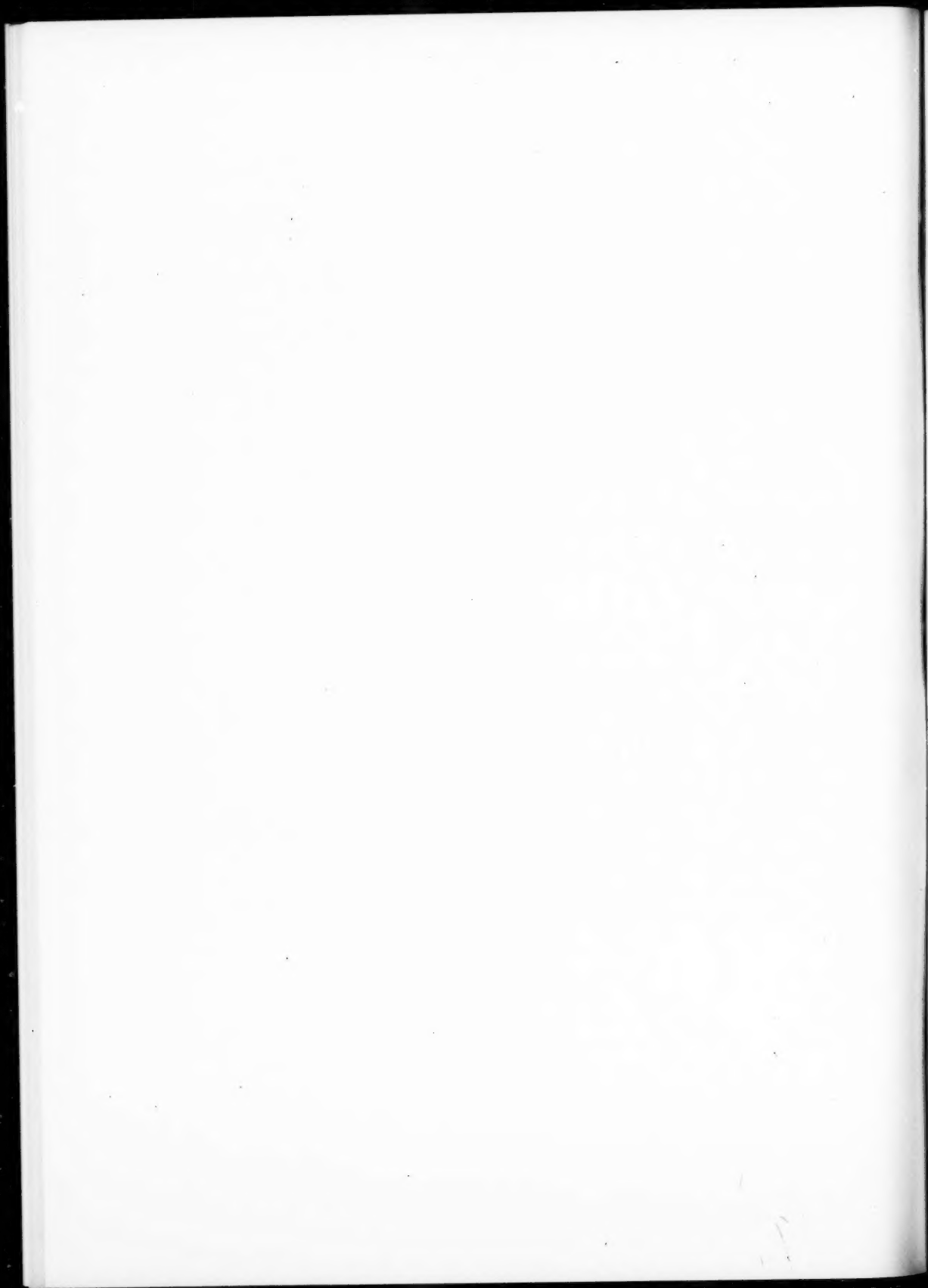
Previous studies of tautomerism (1) have shown that the proton transfer process is quite slow at room temperature and that the lifetime in individual environments is greater than a millisecond. In this case also, the nuclear shielding parameters measured

here would correspond to the azo form only since quadrupole relaxation will prevent detection of a small amount of imino form.

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### *Canadian Journal of Chemistry*

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